Use of PCR in the diagnosis of pericardial amebiasis: a case report and systematic review of the literature

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Abstract
Background: Entamoeba histolytica (E. histolytica) is rarely identified as a cause of amebic pericarditis. We report a case of amebic pericarditis complicated by cardiac tamponade, in which the diagnosis was missed initially and was made retrospectively by polymerase chain reaction (PCR) testing of a stored sample of pericardial fluid. Furthermore, we performed a systematic review of the literature on amebic pericarditis.

Case presentation: A 71-year-old Japanese man who had a history of sexual intercourse with several commercial sex workers 4 months previously, presented to our hospital with left chest pain and cough. He was admitted on suspicion of pericarditis. On hospital day 7, he developed cardiac tamponade requiring urgent pericardiocentesis. The patient’s symptoms temporarily improved, but 1 month later, he returned with fever and abdominal pain, and multiple liver lesions were found in the right lobe. Polymerase chain reaction of the aspiration fluid of the liver lesion and pericardial and pleural fluid stored from the previous hospitalization were all positive for E. histolytica. Together with the positive serum antibody for E. histolytica, a diagnosis of amebic pericarditis was made. Notably, the diagnosis was missed initially and was made retrospectively by performing PCR testing. The patient improved with metronidazole 750 mg thrice daily for 14 days, followed by paromomycin 500 mg thrice daily for 10 days.

Conclusions: This case suggests that, although only 122 cases of amebic pericarditis have been reported, clinicians should be aware of E. histolytica as a potential causative pathogen. The polymerase chain reaction method was used to detect E. histolytica in the pericardial effusion and was found to be useful for the diagnosis of amebic pericarditis in addition to the positive results for the serum antibody testing for E. histolytica. Because of the high mortality associated with delayed treatment, prompt diagnosis should be made.

Keywords: Amebiasis, Pericarditis, Entamoeba histolytica, Polymerase chain reaction

Background
Amebic pericarditis was first reported by Rouis in 1860 during an autopsy of a patient with an hepatic amebiasis [1]. The three stages of amebic pericarditis are (1) “pre-suppurative pericarditis,” an initial sympathetic or reactive effusion, (2) “suppurative pericarditis,” a rupture of a liver lesion into the pericardial cavity with the characteristic anchovy paste appearance, often resulting in cardiac tamponade, and (3) “constrictive pericarditis,” a late complication of amebic pericarditis which develops over weeks to months and requires pericardiectomy [2, 3]. The pre-suppurative form should be considered...
a potential precursor of the suppurative form. Amebic pericardial effusion usually results from the extension of a left lobe liver lesion through the diaphragm into the pericardium, leading to a hepatopericardial fistula [4, 5]. Hematogenous dissemination can also occur, although less frequently.

*Entamoeba histolytica* (*E. histolytica*) is rarely identified as a cause of pericarditis. We report a case of amebic pericarditis in which the cause of the cardiac tamponade was not identified initially, and the diagnosis was made retrospectively when the patient deteriorated 1 month later, by performing PCR on a stored sample of pericardial fluid obtained during the first admission.

**Case presentation**

A 71-year-old man without a history of travel to amebiasis endemic areas presented to our emergency department with a 2-week history of left pleuritic chest pain and a non-productive cough. The patient had a recent past medical history of essential thrombocytopenia and myelodysplastic syndrome/myeloproliferative neoplasm was treated with hydroxyurea (500 mg) followed by anagrelide hydrochloride hydrate (3 mg). Chest radiograph revealed cardiomegaly, pulmonary congestion, and left pleural effusion. The transthoracic echocardiogram (TTE) showed normal left ventricular wall motion with a small amount of pericardial effusion near the left ventricular posterior wall. The patient was admitted to the cardiology department on suspicion of anagrelide-induced acute heart failure; thus, treatment with anagrelide was stopped. The hospital course was favorable until hospital day 9 when the patient developed chest pain and dyspnea. The patient was in severe distress and had a blood pressure of 80/66 mmHg, heart rate of 104 beats per minute, respiratory rate of 24 breaths per minute, and an oxygen saturation of 77% on room air. Electrocardiogram showed ST-segment elevation in V2–6 and PR-segment depression in V3–6. TTE and computed tomography (CT) without contrast showed the increased pericardial fluid effusion. The patient was diagnosed with pericardial tamponade and required an urgent pericardiocentesis. The pericardial fluid was blood-colored with cell count of 4250 cells/µL, predominantly neutrophils (88%) with lymphocytes (6.5%), and eosinophils (0.5%). Many clusters of dead or degenerated cells were observed in cytology as well as in the pericardial fluid. The pericardial cytology, antinuclear antibodies, and IgM antibodies. Moreover, we performed conventional qualitative polymerase chain reaction (PCR) testing of DNA samples extracted from tissue samples of the liver lesion, and pericardial and pleural effusion fluid collected and stored during the first admission, using a dysentery amoeba-specific primer that partially amplified the 18S ribosomal DNA region. The PCR test result was positive. We diagnosed an amebic liver lesion associated with amebic pericarditis. We reported the positive PCR result to the pathologists and asked them to check again, but unfortunately, they could not confirm free living ameba. Of note, the patient initially denied any recent sexual history, but when we interviewed him again after he was diagnosed with amebiasis, he admitted that he had had sexual intercourse with several commercial sex workers 4 months previously. He denied any sexual contact with men, but he stated he had oral-anal sex. The dose of metronidazole was increased (to 750 mg IV every 8 h) and continued for 14 days, followed by oral paromomycin (500 mg every 8 h) for 10 days. The patient was clinically stable and was discharged on day 18 of hospitalization. Follow-up TTE and CT abdomen revealed no evidence of recurrence at the 1-year follow-up.

**Systematic review**

A literature search of the PubMed database (up to November 2019, updated in April 2021) was conducted using the keywords (((“Ameoba”[Mesh] OR amoeba[TIAB] OR ameba[TIAB] OR amebic[TIAB]) OR (“Amebiasis”[Mesh] OR amebias*[TIAB] OR ameobi*[TIAB] OR amoebias*[TIAB])) AND (“Pericarditis”[Mesh] OR pericarditis[TIAB]))) OR (“Heart Diseases/parasitology”[Mesh]) AND (“Ameoba”[Mesh] OR amoeba[TIAB] OR ameba[TIAB] OR amebic[TIAB]) OR (“Amebiasis”[Mesh] OR amebias*[TIAB] OR amoebias*[TIAB])). The Embase database was also searched using the keywords (((“amoeba”/exp OR amoeba) OR ameba
OR amebic OR ‘amebiasis’ OR amebias* OR amoebias*) AND ‘pericarditis’) NOT ((‘amoeba’/exp OR amoeba) OR ameba OR amebic OR ‘amebiasis’ OR amebias* OR amoebias*) AND ‘pericarditis’ AND ([medline]/lim OR [pubmed-not-medline]/lim) (Fig. 1). The database including titles, abstracts, and languages was firstly created by FK using the abovementioned formula. For the literature review, the database records were split in half (A and B). Database A was independently reviewed by KI and RH and database B was independently reviewed by TS and TF. Full-text text was used for eligibility assessment, and detailed information on each case was extracted. Finally, each database was checked by KK and TM to create the combined list of cases. Case reports that were not regarding amoebic pericarditis, and reviews and clinical studies that did not present cases of amoebic pericarditis were excluded. Additionally, reports for which abstracts or full texts were in languages other than English were excluded.

We found 53 papers describing 121 cases of pericarditis caused by *E. histolytica* [1, 3–55]. The detailed information on the clinical characteristics of these 122 cases, which includes our case, are shown in Table 1. Of those cases, 90.4% were male, the median age was 46 years, and only six cases, including this case, were reported after 2000. Moreover, 45.1% (n = 55) of the cases were reported from Asia, followed by Africa (n = 34, 27.9%), Central and South America (n = 11, 9.0%), North America (n = 6, 4.9%), and Europe (n = 3, 2.5%). Liver lesions were noted in 75% (n = 60) of cases, mostly in the left lobe (n = 32, 53.3%), followed by location data not available (n = 20, 33.3%), the right lobe (n = 7, 11.7%), and both lobes (n = 1, 1.7%). Six cases (2.4%) did not have a liver lesion. The median duration of antimicrobial therapy was 14 days, and 31.1% (n = 38) were fatal.

**Discussion and conclusions**

To the best of our knowledge, this is the first systematic review of amebic pericarditis as a rare complication of amebiasis. A strength of this review is that, in addition to providing patient demographics for 122 cases over the past 80 years, it also focuses on the use of PCR, which has recently been shown to be useful for diagnosis for amebiasis. The learning point from this case is that had the diagnosis been made at the time of the first cardiac tamponade, the second hospitalization might have been avoided. The diagnosis was missed initially and confirmed retrospectively when the patient deteriorated 1 month later, by performing PCR on a stored sample of pericardial fluid obtained during the first admission. It is worth noting that although we did not suspect amebiasis because the patient initially denied a history of sexual intercourse and did not have a history of travel to an

![Fig. 1](https://example.com/flowchart.png)
Table 1  Characteristics of patients with amebic pericarditis

| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|----------------|--------------------|-----------------|---------------|------------|-----------|-------------------|----------------------|-------------------|----------|-----------|
| 1   | Laha [6]       | 17  | F   | 1946 | India   | Fever for 2 days | N/A                | N/A             | Yes, R        | The response to treatment | N/A                  | Pericardiocentesis | Emetine 3 g | Cure      | N/A       |
| 2   | Berberian [7]  | 59  | M   | 1949 | The United States | Malaise, weakness, diarrhea | N/A               | N/A             | No           | Biopsy of the wall of the umbilical sinus was positive for E. histolytica | N/A                  | N/A              | Aureomycin | Died      | N/A       |
| 3   | Beemer [8]     | 27  | M   | 1956 | Canada  | Left sided chest pain | N/A                | N/A             | Yes, L        | Autopsy | N/A | N/A              | Streptomycin, isoniazid | N/A | Died      | N/A       |
| 4   | Downie [9]     | 2   | M   | 1960 | Nigeria | Cough, discharging ears, vomiting and diarrhea | None               | None            | Yes, L        | Ameoba was seen in the connective tissue outside the pericardium | N/A                  | N/A              | N/A       | Died      | N/A       |
| 5   | Paulley [5]    | 51  | M   | 1965 | United Kingdom | Burning precordial pain | Ischemic infarction | Residence in India 20 years before admission | Yes, L | The response to treatment | N/A                  | None | Penicillin, chloramphenicol, chloroquine, emetine | Cure | N/A       |
| 6   | Mullan [10]    | 73  | M   | 1965 | United Kingdom | Upper abdominal pain, anoxia, hemoptysis over 1 month | N/A                | N/A             | Yes, R | The presence of confirmed amebic liver abscess and the response to treatment | None (Liver: Actively motile amebae containing red cells, were present) | Pericardiocentesis | Emetine | Died      | None      |
| 7   | Gelfand [11]   | 12  | M   | 1966 | Zimbabwe | Right chest pain for 3 weeks, shortness of breath, weight loss, and fever | None               | None            | Yes, L | Bloodstained fluid, and the response to treatment | Dense fibrous tissue with a sparse chronic inflammatory cellular infiltrate and with a small part of its surface covered by a narrow zone of granulation tissue | Pericardiocentesis | Emetine | Cure     | N/A       |
| 8   | Kulpati [12]   | 23  | M   | 1966 | India   | Prexia, upper abdominal pain, constipation | N/A                | N/A             | Yes          | Liver aspiration contained trophozoites of E. histolytica | N/A                  | Yes, but not mentioned in detail | Cure | No recurrence 4 month after discharge | N/A       |
| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|----------------|--------------------|---------------|--------------|-----------|-----------|---------------------|---------------------|-----------------|----------|----------|
| 9   | D’cruz [13] | 21  | M   | 1967 | India   | Severe retrosternal pain, vomited and fainted | N/A | N/A | Yes | Pericardial fluid contained trophozoites of *E. histolytica* | N/A | None | No | Died | N/A |
| 10  | Rab [14]    | 49  | M   | 1967 | Pakistan | Retrosternal pain, dyspnea | N/A | N/A | Yes, L | Anchovy sauce pus and the response to treatment | Fibrous deposit | Pericardiocentesis | N/A | Died | None |
| 11  | Cook [15]   | 25  | M   | 1970 | Malaysia | Fever, cough, bloody sputum | None | N/A | Yes, R | The response to emetine and a strongly positive amebic fluorescent antibody test | None | Pericardiocentesis, laparotomy of left subphrenic abscess | Emetine and chloroquine | Cure | N/A |
| 12  | Ganeshananthan [16] | 36 | M   | 1971 | Sri Lanka | Dry cough and chest pain for 3 weeks | N/A | N/A | N/A | Thick brown pus, having the consistency of typical amoebic liver abscess pus | N/A | Pericardiocentesis | Emetine, metronidazole, chloroquine | Cure | No recurrence 3 years after discharge |
| 13  | Bansal [17] | 19  | M   | 1971 | India   | Fever, dry cough, right shoulder pain for 5 days | N/A | N/A | Yes, R | Anchovy sauce pus and the response to treatment | None | Pericardiocentesis | Emetine, chloroquine, di-iodohydroxy quinoline | Cure | No recurrence 16 months after discharge |
| 14  | Kapoor [18] | 27  | M   | 1972 | India   | High fever with pain in the left chest and subcostal region | Gastro-pericardial fistula | N/A | Yes, L | N/A (Stool: trophozoites of *E. histolytica*) | N/A | Pericardiocentesis | Intramuscular emetine | Cure | NA |
Table 1 (continued)

| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|----------------|--------------------|-----------------|--------------|------------|-----------|---------------------|----------------------|-------------------|----------|
| 15  | Kapoor [18]    | 30  | M   | 1972 | India   | General weakness, pain in the abdomen and swelling in the epigastrium for 3 weeks | N/A | N/A | Yes, L | N/A (Stool: trophochozites of E. histolytica) | Pericardiocentesis | Emetine, chloroquine | Cure    | N/A       |
| 16  | Kapoor [18]    | 34  | M   | 1972 | India   | Pain in the epigastrium and right lumbar region for 2 months | N/A | N/A | Yes | Anchovy sauce pus from the front of pericardial cavity | Pericardiocentesis, thoracotomy | Emetine | Cured   | N/A       |
| 17  | Kapoor [18]    | 35  | M   | 1972 | India   | Sudden onset of severe generalized chest pain and dyspnea for 12 h | N/A | N/A | Yes, L | N/A (Liver: trophochozites of E. histolytica) | Pericardiocentesis | N/A | Died    | N/A       |
| 18  | Kapoor [18]    | 25  | M   | 1972 | India   | Pyrexia for 5 days | N/A | N/A | N/A | N/A | Pericardiocentesis | Dehydroemetine, chloroquine | Cured | No recurrence 3 weeks after discharge |
| 19  | Kapoor [18]    | 50  | M   | 1972 | India   | Fever for 2 months and pain in the right hypochondrium | N/A | N/A | Yes, L | Anchovy sauce pus from the pericardial cavity | Pericardiocentesis | Emetine, chloroquine | Cured | No recurrence two years after discharge |
| 20  | Spiegel [19]   | 48  | M   | 1972 | The United States | Abdominal pain of right upper quadrant | N/A | N/A | Yes, R | Pericardial fluid contained trophochozites of E. histolytica | N/A | Metronidazole and chloroquine | Cure | N/A       |
| 21  | Heller [20]    | 42  | F   | 1972 | United States | Dyspnea, weight loss, left upper abdominal pain for 8 days | N/A | Move from Mississippi to Chicago when she was 3 years old | Yes, L | Anchovy sauce pus, the response to treatment, and indirect hemagglutination test (1:2560) | Fibrinous pericarditis | Pericardiocentesis followed by pericardectomy | Metronidazole 750 mg thrice daily for 3 weeks | Cure | N/A       |
| No. | Case reference | Age | Sex | Year | Country    | Chief complaint                                                                 | Underlying diseases | Travel history | Liver abscess | Diagnosis                  | Biopsy findings                                      | Surgical intervention       | Antimicrobial used               | Outcome       | Follow up                      |
|-----|----------------|-----|-----|------|------------|----------------------------------------------------------------------------------|---------------------|----------------|--------------|----------------------------|-----------------------------------------------|-----------------------------|-----------------------------|--------------|-------------------------------|
| 22  | Heller [20]    | 47  | M   | 1972 | United States | Retrosternal pain, sweating, dyspnea for 1 day                                    | N/A                 | Move from Mexico to Chicago 5 months previously | Yes, L       | Anchovy sauce pus, the response to treatment, and indirect hemagglutination test (1:5128) | Fibrous pericarditis                  | Pericardiectomy                | Emetine (next day changed to dehydroemetine), chloroquine | Died          | None                          |
| 23  | Anderson [21]  | N/A | M   | 1972 | United States | Left pleuritic chest pain, jaundice for 10 days                                  | None               | N/A            | Yes, L       | Anchovy sauce pus and the response to treatment | None                             | Pericardiocentesis followed by pericardiectomy | N/A           | Cure                          |
| 24  | Suryanarayan [22] | 40  | M   | 1973 | India       | Pain in the epigastic region and hypochondrium for one month, and dyspnea for 1 week | N/A                 | N/A            | Yes, L       | N/A                        | N/A                             | Pericardiocentesis               | Dehydroemetine, tetracyclines, chloroquine and didoquin | Cure          | N/A                           |
| 25  | Suryanarayan [22] | 45  | M   | 1973 | India       | Fever for 3 months and dyspnea for 2 days                                       | N/A                 | N/A            | Yes, L       | Pericardial fluid contained trophozoites of E. histolytica | N/A                             | None                        | N/A           | Died                          |
| 26  | Lewis [23]     | 35  | M   | 1973 | N/A         | N/A                                                                              | N/A                 | N/A            | N/A         | N/A                        | The fluorescent antibody test was positive | None                        | N/A            | N/A           | No recurrence 6 months after discharge |
| 27  | Ganeshananthan [16] | 33  | M   | 1974 | Sri Lanka   | Left-sided chest pain and shortness of breath for 2 weeks                       | N/A                 | N/A            | N/A         | N/A                        | Pericardiocentesis               | Emetine, metronidazole     | N/A           | Cure                         |
| 28  | Ganeshananthan [16] | 43  | M   | 1974 | Sri Lanka   | Shortness of breath and pain in the chest and abdomen for 18 days               | N/A                 | N/A            | Yes          | Typical amoebic pus was drawn out from needle of the pericardium | None                             | Pericardiocentesis               | Emetine, tetracycline, metronidazole | Cure           | N/A                           |
| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|----------------|-------------------|----------------|-------------|-----------|------------|------------------|---------------------|----------------|----------|
| 29  | Ganeshanathan [16] | 32  | N/A | 1974 | Sri Lanka | Pain in the left upper abdomen for 2 months | N/A | N/A | N/A | The fluorescent antibody test was positive | None | Pericardiocentesis | Emetine and chloroquine followed by metronidazole | Cure | N/A |
| 30  | Guimaraes [24] | 33  | M   | 1974 | Brazil | Fever, chills, dry cough, retrosternal pain, weight loss, dyspnea, diarrhea | N/A | N/A | Yes, L | Anchovy sauce pus and the response to treatment | None | Pericardiocentesis | Chloroquine 2 g daily for 7 days, followed by 500 mg daily for 23 days, metronidazole 2 g daily for 30 days, emetine hydroxychloroquine 60 mg daily for 10 days plus the injection of 7.5% hypaque into the pericardial cavity | Cure | N/A |
| 31  | Faerber [25] | 35  | M   | 1974 | South Africa | Pleuritic chest pain, productive cough, hemoptysis for 2 months | N/A | N/A | Yes, R and L | None | Pericardiocentesis | Dehydroemetine, metronidazole | Cure | N/A |
| 32  | Haranath [26] | 55  | M   | 1974 | India | Exertional dyspnea, distention of the abdomen and edema of the left upper limb for 10 days | Rheumatic fever | N/A | N/A | Anchovy sauce pus from the cardiac cavity | None | Pericardiocentesis | Dehydroemetine, metronidazole | Cure | NA |
| 33  | Ganesan [3] | 40  | M   | 1975 | India | Progressive general weakness, chest pain, dyspnea for 20 days | N/A | N/A | Yes, L | Anchovy sauce pus and the response to treatment | None | Pericardiocentesis | Dehydroemetine 30 mg daily for 10 days, chloroquine 250 mg thrice daily for 10 days, and metronidazole 1200 mg daily for ten days | Cure | N/A |
Table 1 (continued)

| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|-----------------|--------------------|-----------------|--------------|-----------|----------------|-----------------------|------------------|----------|-----------|
| 34  | Agrawal [1]    | 40  | M   | 1975 | India   | Fever, cough, pain in right hypochondrium, fatigue for 2 months | None               | N/A             | Yes, L       | Aspiration of anchovy source pus from the cardiac cavity | The nonspecific chronic inflammatory reaction of the pericardium | Pericardiocentesis | Metronidazole | Died      | None      |
| 35  | Agrawal [1]    | 25  | N/A | 1975 | India   | Pain in the upper abdomen and dry cough for 2 weeks | None               | N/A             | Yes, L       | Aspiration of anchovy source pus from the cardiac cavity | An actively inflamed fibrosing pyopericardium of nonspecific nature | Pericardiocentesis | Metronidazole | Cure      | No recurrence after discharge |
| 36  | Kulpati [27]   | 34  | M   | 1976 | India   | Moderately high intermittent fever and dull aching pain in right hypochondrium for 1 month | History of amoebic dysentery about 8 months back | N/A             | Yes, L       | The pericardial fluid was chocolate colored. The direct smear and culture of pericardial fluid demonstrated *E. histolytica* | N/A | Pericardiocentesis | Metronidazole and emetine | Emetine, metronidazole, and tetracycline | Died | N/A |
| 37–63 | Adams EB1-27 [28] | N/A | N/A | 1977 | South Africa | Pyrexia and pain in the right upper abdomen for 2 weeks and breathlessness for 4 days | None | N/A | N/A | 8 patients (mostly L) | N/A | N/A | N/A | Cure (n = 19) Died (n = 8) |
| 64  | Muralidar [29] | 19  | F   | 1977 | India   | Chest pain and breathlessness since 3 days | History of amoebic dysentery | N/A             | N/A | Anchovy sauce pus from the cardiac cavity | N/A | Pericardiocentesis | Emetine and metronidazole | Cure | Died | N/A |
| 65  | Muralidar [29] | 52  | M   | 1977 | India   | History of amoebic dysentery | N/A             | N/A | N/A | Anchovy sauce pus from the cardiac cavity, serum indirect hemagglutination | N/A | Pericardiocentesis | Emetine and metronidazole | Cure | No recurrence after discharge |
| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|----------------|-------------------|----------------|-------------|-----------|-----------|-------------------|---------------------|-----------------|-----------|
| 66  | Kundu [30]     | 25  | F   | 1978 | India   | Pain in right hypochondrium associated with moderately high intermittent fever for 15 days and difficulty in breathing for 1 week | None | N/A | Yes, L | Serum gel diffusion test, chocolate pus | N/A | Pericardiocentesis | Metronidazole followed by chloroquine | Cure | No recurrence 4.5 months after discharge |
| 67  | Bellosillo [31] | 37  | M   | 1978 | Philippine | Shortness of breath | None | N/A | Yes | Pericardial fluid contained trophozoites of E. histolytica | N/A | Pericardiocentesis | Tinidazole | Cure | No recurrence 3 months after discharge |
| 68–72 | Vergheze 1-5 [32] | N/A | N/A | 1979 | India | N/A | N/A | N/A | N/A | N/A | Pericardiocentesis (n = 1), pericardiotomy (n = 3) | N/A | Cure (n = 3), Died (n = 2) | N/A |
| 73  | Almeida [33]   | 35  | M   | 1979 | India | Epigastric pain for 1 month and swelling in upper abdomen for 15 days | None | N/A | Yes, L | Anchovy sauce pus and the response to treatment | N/A | Pericardiocentesis | Emetine and chloroquine | Cure | No recurrence 9 months after discharge |
| 74  | Almeida [33]   | 20  | M   | 1979 | India | Shortness of breath and left chest pain for 3 days | None | N/A | Yes, L | Anchovy sauce pus from the cardiac cavity | Yes, L | Pericardiocentesis | Emetine, and oxytetracycline | Died | N/A |
| 75  | Almeida [33]   | 25  | M   | 1979 | India | Left chest pain, cough, and fever for 1 month | None | N/A | Yes, L | Anchovy sauce pus from the cardiac cavity | N/A | Pericardiocentesis | N/A | Died | N/A |
| 76  | Almeida [33]   | 40  | M   | 1979 | India | Anorexia, fever, and right chest pain for 15 days | None | N/A | Yes, L | Autopsy revealed liver abscess with pericarditis and cardiac tamponade | N/A | None | N/A | Died | N/A |
| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|-----------------|--------------------|---------------|--------------|-----------|---------------|------------------------|-------------------|----------|----------|
| 77  | Almeida [33]   | 50  | F   | 1979 | India   | Jaundice and fever for 1 month | None              | N/A           | Yes, L      | Bloodstained fluid | N/A | Pericardiectomy | Emetine and metronidazole | Died             | N/A      |
| 78-89 Tyagi 1–12 [34] | 4–55 | M9: F:3 | 1980 | India | Fever (n= 10), dyspnea (n= 5), cough (n= 4), diarrhea (n= 3) | N/A | N/A | Yes, L; 5, R: 4 | Anchovy sauce pus from the cardiac cavity (n= 2), pericardial fluid contained trophozoites of E. histolytica (n= 2) | N/A | Pericardiocentesis | N/A | Cure (n= 4) | Died (n= 8) |
| 90  | Gupta [35]     | 43  | M   | 1980 | India   | Dyspnea, chest pain | N/A | N/A | No | Pericardial fluid contained trophozoites of E. histolytica | N/A | Pericardiocentesis | N/A | Cure | N/A |
| 91  | Kala [36]      | 35  | M   | 1980 | India   | Dyspnea, diarrhea | N/A | N/A | Yes | Pericardial fluid contained trophozoites of E. histolytica | N/A | Pericardiocentesis followed by pericardectomy | Emetine, Streptomycin, Isoniazid | Cure | N/A |
| 92-101 Ibarra-Perez 1–10 [37] | N/A | N/A | 1981 | Mexico | N/A | N/A | N/A | N/A | None | Pericardectomy | N/A | N/A | N/A | N/A | N/A |
| 102 | Adeyemo [38]   | N/A | N/A | 1984 | Nigeria | N/A | N/A | N/A | Yes, L | N/A | N/A | Pericardiocentesis | N/A | Died | N/A |
| 103 | Adeyemo [38]   | N/A | N/A | 1984 | Nigeria | N/A | N/A | N/A | Yes, L | N/A | N/A | Pericardiocentesis | N/A | Died | N/A |
| 104 | Farer [39]     | 23  | M   | 1984 | Vietnam | Dyspnea, chest pain | N/A | Indonesia | N/A | Microscopic finding of amebic trophozoites, anchovy sauce pus, and the response to treatment | None | Pericardiocentesis | Specific chemotherapy for amebiasis | Cure | N/A |
| No.   | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-------|----------------|-----|-----|------|---------|-----------------|--------------------|---------------|--------------|-----------|------------|---------------------|---------------------|----------|-----------|
| 105   | Shanker [40]   | 30  | M   | 1985 | India   | Irregular fever and dull aching pain in right hypochondrium for 1 month | History of amoebic dysentery about 6 months back | N/A           | N/A         | Pericardial fluid contained trophozoites of E. histolytica | Autopsy            | N/A      | Metronidazole, ampicillin, emetine hydrochloride | Cure               | N/A       |
| 106   | Pirie [41]     | N/A | N/A | 1986 | South Africa | N/A             | N/A               | N/A           | N/A         | N/A      | N/A       | N/A                 | N/A                 | N/A      | N/A       |
| 107   | Baid [42]      | 48  | M   | 1987 | India   | Dyspnea, left chest pain, fever, edema of the feet, weakness for 1 month | N/A               | N/A           | Yes, R      | Anchovy sauce pus and the response to treatment | Subepicardial fat-containing proliferating fibroblasts and lymphocytic infiltrate | Pericardiocentesis followed by pericardectomy | Metronidazole       | Cure       | None     |
| 108   | Strang [43]    | N/A | N/A | 1987 | South Africa | N/A             | N/A               | N/A           | Yes         | The positive serological tests (1/1024) for amoebiasis, the appearance of the fluid obtained on tapping the pericardium, and the response to treatment | None               | N/A      | Metronidazole and chloroquine | Died               | None      |
| 109   | Blackett [44]  | 50  | M   | 1988 | Cameroon | Left-sided chest pain, dyspnea, abdominal distension, edema for several days | N/A               | N/A           | None        | None      | None      | None                | None               | Metronidazole and chloroquine | Died               | None      |
| 110   | Vanachayangkul [45] | 51  | M   | 1989 | Thailand | Epigastric oppression and fever for 1 week beginning with severe pain, occasionally colicky in nature without nausea or vomiting | N/A               | N/A           | Yes         | Aspiration of pericardial effusion yielded 350 mL of brownish grey pus with numerous trophozoites of active motile E. histolytica | Pericardiocentesis is followed by pericardiotomy | N/A      | Metronidazole and amikacin | Cure               | N/A       |
| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|----------------|--------------------|---------------|--------------|-----------|-----------|-------------------|---------------------|------------------|----------|-----------|
| 111 | Lami [46]      | 26  | F   | 1989 | Italy   | Fever, headache, chest pain | None               | N/A           | None         | Indirect hemagglutination test | N/A                  | N/A              | Metronidazole 2 g daily for 10 days | Cure     | N/A |
| 112 | Supe [47]      | 40  | M   | 1991 | India   | N/A | N/A | N/A | Yes | E. histolytica antibody was positive | None                  | N/A              | Pericardioscrisis | Emetine, metronidazole and amikacin | Cure     | N/A |
| 113 | Gomersall [48] | 28  | M   | 1994 | United Kingdom | Fever, right sweats, pyrexia, and right-sided pleuritic chest pain for 6 weeks | None         | Stationed in Kenya | Yes, L | A fluorescent antibody test for E. histolytica was positive (titer 1/320) and amoebic enzyme immunoassay was positive at 120% | None                  | Pericardioscrisis | Metronidazole for 10 days and diloxanide for 10 days | Cure     | No recurrence 6 months after discharge |
| 114 | Perna [49]     | 37  | M   | 1994 | Italy   | Fever, malaise, weight loss | Drug addiction | N/A | Yes, L | A bacteriological specimen from the pericardial fluid yielded E. histolytica, anchovy sauce pus, and the response to treatment | N/A                  | Pericardioscrisis | Chloroquine | N/A |
| 115 | Shandera [50]  | 64  | M   | 1998 | India   | Epigastric pain and pleuritic pain for 6 weeks | N/A               | N/A           | Yes, L | Positive serological tests for amoebiasis | None                  | Pericardioscrisis | Metronidazole and diiodoquinol | Cure     | N/A |
| 116 | Chao [4]       | 44  | M   | 1998 | Taiwan  | Dyspnea for the previous 2 days, mucoid diarrhea for 3 days | Chronic schizophrenia | N/A           | Yes, L | Amoebic antibodies by hemagglutination test (1:1,6384) | None                  | Pericardioscrisis | Metronidazole 500 mg daily for 2 weeks | Cure     | No recurrence 1-year after discharge |
| 117 | Wiwanitkit [51]| N/A | N/A | 2008 | Thailand | Chest pain, discomfort, and anpharhythmia | N/A               | N/A           | Yes | None | None | None                  | N/A                  | Cure (n = 2) | Died (n = 1) | N/A |

Table 1 (continued)
| No. | Case reference | Age | Sex | Year | Country | Chief complaint | Underlying diseases | Travel history | Liver abscess | Diagnosis | Biopsy findings | Surgical intervention | Antimicrobial used | Outcome | Follow up |
|-----|----------------|-----|-----|------|---------|-----------------|---------------------|-----------------|--------------|-----------|-----------|-------------------|---------------------|---------------|----------|
| 118 | Murali [52]   | 38  | M   | 2011 | India   | Fever and right hypochondral pain for 10 days | N/A                  | N/A             | Yes, R       | Positive linked immunosorbent assay for E. histolytica (both IgM and IgG) | None                | Pericardiocentesis | Meropenem, metronidazole | Cure          | N/A       |
| 119 | Amine [53]    | 38  | M   | 2015 | Morocco | Fever, shortness of breath, and leg swelling for 2 months | Recurrent diarrhea | N/A             | None         | Trophozoites of E. histolytica (pleural effusion) | None                | Pericardiectomy | Metronidazole 500 mg trice daily | N/A           | N/A       |
| 120 | Agarwal [54]  | 25  | M   | 2019 | India   | Abdominal pain and fever for 1 month | None                | N/A             | Yes, L       | Anchovy sauce pus, PCR for E. histolytica from the pericardial cavity | N/A                | Pericardiocentesis, pleural pericardial window | Metronidazole | Cure          | No recurrence at 1 year after discharge |
| 121 | Keleş [55]    | 25  | M   | 2020 | India   | Fever, chills, and pain in the upper abdomen for 1 month | N/A                | N/A             | Yes, L       | Reddish-brown pus from the cardiac cavity, positive serological test for amebiasis, and PCR for E. histolytica | N/A                | Pericardiocentesis | Metronidazole followed by oral luminal amebicide diloxanide | Cure          | No recurrence 1-year after discharge |
| 122 | Francis [56]  | 15  | M   | 2020 | Turkey  | Diarrhea and abdominal pain for 2 days | None                | N/A             | None         | E. histolytica trophozoites and cysts in fresh stool, and the response to treatment | None               | None | Metronidazole (30 mg/kg/day) | Cure          | No recurrence 6-month after discharge |
| 123 | Raza [57]     | 7   | M   | 2020 | Pakistan | Fever and abdominal pain for 15 days and diarrhea for 3 days | Acute gastroenteritis | N/A            | Yes, L       | Cysts of E. histolytica and positive enzyme-linked immunosorbent assay in stool | None               | None | Metronidazole for 14 days, followed by diloxanide furoate for the next 7 days | Cure          | No recurrence 2-week after discharge |
endemic area. We learned that if the cause of pericarditis is unclear, a detailed interview should be conducted and amebiasis should be suspected.

Most cases of amebic pericarditis were reported from developing countries, especially the tropics and subtropics in Asia and Africa, where there is inadequate hygiene and access to sanitation [58]. This trend is similar to that of all amebic dysentery and amebic liver lesion [58]. The previous study in Egypt showed that approximately 40% of patients with acute diarrhea had amebic colitis [59]. The reason why the number of case reports peaked in the 1970s and has been gradually decreasing subsequently, may be because treatment has been standardized and is generally successful, so clinicians are less likely to report cases. In developing countries where amebiasis are endemic, it is still possible that this has not yet been reported due to underdevelopment of surveillance and diagnostic techniques [58]. Even not in endemic areas, as our case, sexual intercourse could be the risk factors of amebiasis.

Regarding the location of the liver lesion, in our literature review, we found that 32 cases (53.3%) had left lobe liver lesion, seven (11.7%) with only right lobe liver lesion, and six case (2.4%) without a liver lesion was observed. Although it has been known that amebic pericarditis is often associated with left-sided liver lesions, this result suggested that amebic pericarditis is not necessarily only secondary to the left lobe of the liver. The absence of an initial liver lesion in our case made the diagnosis of amebic pericarditis difficult, but this case taught us that PCR testing for amebiasis should be performed promptly when investigating cases of pericarditis of unknown origin. The fact that the pericarditis preceded the liver lesion in our case, and that the pericardial fluid was bloody, not like anchovy paste, suggests that the mechanism of spread to the pericardium was by hematogenous dissemination. Anchovy paste-like liquid is seen in cases of liver lesion, and consists of ameba bound to necrotic liver cells. In fact, considering that other extraintestinal amebiasis, such as central nervous system lesions and pulmonary amebiasis without liver lesions are assumed to be disseminated hematogenously [58, 60], trophozoites could have disseminated into the pericardial sac via the bloodstream.

In terms of diagnosis, anchovy paste-like fluid by pericardiocentesis was reported to be the main characteristic and was found in about half of the cases evaluated in this review. Since the 1970s, there has been an increase in the number of cases in which a positive antibody test was combined with pericardiocentesis [3, 18]. Until then, most cases had been clinically diagnosed only by the characteristic pericardial fluid findings of “anchovy paste” and response to treatment. Considering that
trophozoites could be seen microscopically in only two cases (7.1%), the absence of trophozoites could not rule out amebic pericarditis. Notably, the most recent reports revealed the usefulness of PCR detection of *E. histolytica* in pericardial fluid [49, 51]. Since PCR for *E. histolytica* has been reported to be useful in intestinal and extraintestinal amebiasis [61], clinicians should consider using PCR methods to confirm *E. histolytica* in patients with pericarditis of unknown origin.

The conventional qualitative PCR method used in this study has been shown to be highly specific and sensitive by testing with DNA from a variety of pathogens, including bacteria and other protozoa [62]. Unfortunately, we did not perform serum quantitative PCR in this case. It would have been informative to compare the results of serum quantitative PCR between first and second admissions. Compared with conventional PCR, real-time PCR has the following advantages: (1) the results are easier to interpret numerically than by visually checking the stained gels as in conventional PCR; (2) the sensitivity is higher; (3) no post-amplification analysis is required, minimizing the risk of contamination of the laboratory; (4) the duplex profile can distinguish between *E. histolytica* and *E. dispar* infections [63]. Nevertheless, real-time PCR is more costly than morphological stool examination and antigen-based detection tests. Therefore, real-time PCR is unaffordable in many of the countries in which *E. histolytica* is endemic. Instead, this technique may be useful in developed countries for diagnosing amebiasis in travelers from endemic areas.

Our literature review showed that, in most cases, pericardiocentesis was performed to investigate the cause of pericarditis. However, as in our case, it is essential to note that cardiac tamponade may occur, requiring urgent puncture or pericardiotomy. In this review, approximately 30% of patients died. In patients with tamponade early surgical intervention is essential, regardless of the cause. Regarding antimicrobial options, metronidazole was most commonly used, followed by emetine. The dosage and optimal duration of metronidazole varied widely. Still, as recommended for other amebic infections [58], most of the patients received 500–750 mg three times a day for 10–14 days (median = 14 days).

An important limitation of this study is that many of the cases were old and could not be directly compared due to differences in diagnostic tools. Due to the unavailability of accurate diagnostic tests, there are likely to have been many additional cases that were not diagnosed or reported. Furthermore, it should be noted as a limitation that manuscripts published in languages other than English are excluded in this review, as shown in Fig. 1. There may be differences in the characteristics of amoebiasis in countries where English is not the native language.

Moreover, the recurrence rate or long-term prognosis could not be determined because of a lack of information. Further cases should be accumulated, and research on the appropriate diagnosis and management of amebic pericarditis is warranted.

In summary, although amebic pericarditis is rare, it should be promptly diagnosed and treated because of its high mortality rate. In addition to serum antibodies, PCR obtained by pericardiocentesis should be considered for patients with pericarditis of unknown origin and high pretest probability. It is also important for clinicians to be aware that pericarditis can be associated not only with the typical left lobe, but also with the right lobe, in the absence of liver lesion, or with delayed appearance, as in our case. This study highlights amebic pericarditis and contributes to the knowledge of its diagnosis.

**Abbreviations**
CK: Creatine kinase; CT: Computed tomography; *E. histolytica*: Entamoeba histolytica; IV: Intravenous; PCR: Polymerase chain reaction; TTE: Transthoracic echocardiogram.

**Acknowledgements**
We would like to thank Editage (www.editage.com) for English language editing.

**Authors’ contributions**
TM drafted the manuscript. AS, FK, TA, AM, NK, KY, YU, and NM supervised and edited the manuscript. FK, KI, RH, TS, TF, and KK participated in the literature review. KY analyzed the serum antibodies and PCR for amebiasis. All authors reviewed the final manuscript and approved its contents. All authors read and approved the final manuscript.

**Funding**
There were no sources of funding used in the conception, composition, editing, or submission of this manuscript.

**Availability of data and materials**
Not applicable.

**Declarations**

**Ethics approval and consent to participant**
Not applicable

**Consent to publish**
Written informed consent was obtained from the patients in this case report.

**Competing interests**
Yuki Uehara is a member of the editorial board. The other authors declare that they have no competing interests.

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**Received:** 12 April 2021  **Accepted:** 19 August 2021  
**Published online:** 16 September 2021
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