# Hematogenic hepatic abscess in a patient presenting fever of unknown origin

*Abscesso hepático de origem hematogênica em paciente com febre de origem indeterminada*

*Absceso hepático de origen hematogénico en paciente con fiebre de origen indeterminado*

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**ABSTRACT**

**Objective**: To describe the clinical presentation of an atypical liver abscess in the pediatric setting and to conduct a review of the literature concerning ethiopathogenic differences between developed and developing countries.

**Case description**: A 13-year-old male patient was admitted to the emergency room due to daily fever and weight loss, without abnormalities in his physical examination. After undergoing an investigation, the patient was found to have a well-defined heterogeneous nodular area in the abdominal ultrasonography exam, which was compatible with liver abscess. He was subsequently submitted to surgical drainage and started on antibiotics. The drainage material culture turned positive to methicillin-sensible *Staphylococcus aureus.*

**Comments**: The present case report shows that the pediatrician needs to be aware of the common causes of fever of unknown origin in order to systematically develop an investigative approach. In face of the diagnosis of a liver abscess, the possibility of *Staphylococcus aureus*, especially with a previous history of skin rupture, should be considered.

**Key-words**: liver abscess; fever of unknown origin; *Staphylococcus aureus*.

**RESUMO**

**Objetivo**: Descrever uma apresentação atípica de abscesso hepático em paciente pediátrico e realizar uma revisão da literatura no que diz respeito às diferenças observadas na etiopatogenia do quadro, quando considerados os países desenvolvidos e aqueles em desenvolvimento.

**Descrição do caso**: Paciente de 13 anos, do sexo masculino, foi trazido ao pronto-socorro pediátrico devido à febre diária e à perda de peso, sem alterações ao exame físico. Na investigação realizada, o ultrassom abdominal evidenciou área heterogênea nodulariforme relativamente definida, compatível com abscesso hepático. Foi realizada drenagem cirúrgica e antibioticoterapia. No material da drenagem houve crescimento de *Staphylococcus aureus* sensível à oxacilina.

**Comentários**: O caso demonstra a importância de o pediatra conhecer as principais causas da febre de origem indeterminada, saber desenvolver a abordagem investigativa e, frente ao diagnóstico de abscesso hepático, aferir a possibilidade de o agente etiológico ser o *Staphylococcus aureus*, principalmente quando houver relato de rotura da pele.

**Palavras-chave**: abscesso hepático; febre de causa desconhecida; *Staphylococcus aureus*.

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**RESUMEN**

**Objetivos:** Describir una presentación atípica de absceso hepático en pacientes pediátricos y realizar una revisión de la literatura en lo que se refiere a las diferencias observadas en la etiopatogenia del cuadro, cuando considerados los países desarrollados y en desarrollo.

**Descripción del caso:** Paciente de 13 años, varón, fue traído a la emergencia pediátrica debido a la fiebre diaria y pérdida de peso, sin alteraciones al examen físico. En la investigación realizada, el ultrasonido abdominal evidenció área heterogénea nodulariforme relativamente definida, compatible con absceso hepático. Se realizó drenaje quirúrgico y antibioticoterapia. En el material drenado hubo crecimiento de *Staphylococcus aureus* sensible a la oxacilina.

**Comentarios**: El caso demuestra la importancia del pediatra en conocer las principales causas de fiebre de origen indeterminado, en saber desarrollar un acercamiento investigativo y, frente al diagnóstico de absceso hepático, estimar la posibilidad de que el agente etiológico sea el Staphylococcus aureus, principalmente cuando haya relato de rotura de la piel.

**Palabras clave:** absceso hepático; fiebre de causa desconocida; *Staphylococcus aureus*.

## Introduction

Liver abscesses, at a rate of 2.3 to 20 cases per 100,000 inhabitants[1-3], are relatively rare in the general population. In spite of that, this pathology is relevant because of its associated mortality, which ranges from 2 to 12%[3,4].

Its prevalence is higher among adults than among children, and it affects more men than women (3.3 *versus* 1.3 for 100,000 inhabitants)[2,5]. In adults, the main risk factors are associated with liver transplants[2], malignant and benign pathologies of the biliary duct[1,5], neoplasia[2] and diabetes mellitus[2,5]. Among children, other diseases may also be associated: innate immunity disorders, Crohn's disease and intra-abdominal sepsis[6]. In children, the epidemiology of liver abscesses in developing countries is different from that seen in developed countries, where it is rare and usually associated with a primary disease that results in immunodepression, such as chronic granulomatous disease. About one third of the children with chronic granulomatous disease have a liver abscess some time in their life[7]. A recent study in the United Kingdom reported on the occurrence of 15 cases of pyogenic liver abscess in ten years, and in 20% of the cases the liver abscess was the first sign of chronic granulomatous disease[6]. In developing countries, the prevalence of liver abscess is significantly higher. A three-year study conducted in Brazil by Ferreira *et al*[8] found 65 cases of liver abscess in children, and at least 35% of them were associated with skin lesions. In the same study, results of stool examination were available for 36 of the 65 cases, and helminth infection was found in 32, whereas only one had an *Entamoeba histolytica* cyst. These data suggest that helminth infection may play an important role in the etiopathogenesis of the disease, whether amebiasis seems to be a rare cause of liver abscess in the Southern and Southeastern regions of Brazil. The occurrence of helminth infection has also been identified as a predisposing factor by other authors[9].

A history of trauma was found in 3% of the cases by Ferreira *et al*[8]. No risk factors were detected in 46% of the population under study[8], in agreement with other studies in the literature, which reported that no cause could be defined in 50% of the cases of liver abscess[10,11]. The main etiologic agents for liver abscess are different for adult and pediatric populations. Among adults, a substantial number of pyogenic abscesses have a polymicrobial origin, including aerobic and anaerobic bacteria. The main agents are *Klebsiella pneumoniae* (27 to 82%) and *Streptococcus milleri* (44%)[1,2,5], whereas the presence of *Staphylococcus aureus* is rare (6%)[2]. However, among children, *Staphylococcus aureus* is the most common etiologic agent, accounting for 20 to 55% of the cases[6,8].

The clinical signs and symptoms of patients with a liver abscess include fever in about 89% of the cases, abdominal pain in 55 to 72%, and chills in 49 to 69%[1,2]. Unspecific symptoms, such as nausea, vomits, anorexia and weight loss[1,3,12], are also frequent. Physical examination often reveals liver tenderness (55%), jaundice (50%) and hepatomegaly (35%)[1].

This study describes the clinical presentation of a pediatric patient with an atypical liver abscess and reviews the literature about the differences in the etiopathogenesis of this disease in developed and developing countries.

## Case report

A 13-year-old boy, followed up as an outpatient in the Pulmonology and Neurology Services due to asthma and attention deficit hyperactivity disorder, was regularly taking methylphenidate and valproic acid. The patient was brought to the pediatric emergency department due to daily fever of

**Table 1 -** Radiography and laboratory tests

| | 20th day with fever Outpatient service | 25th day with fever Emergency Department | 15th hospitalization day Ward |
|---|---|---|---|
| Hb/Ht (g/dL – %) | 10.7/33.0 | 10.8/34.5 | |
| Leukocytes (µL) | 17,400 | 17,100 | |
| Platelets (K/µL) | 405,000 | 426,000 | |
| CRP/ESR (mg/dL and mm) | 161/- | 153/55 | |
| LDH/uric acid (U/L – mg/dL) | | 159/3.6 | |
| Cytomegalovirus test | | Positive IgG and IgM negative IgM | |
| Epstein Barr Virus test | | Positive IgG and IgM negative IgM | |
| Toxoplasmosis test | | Negative IgG and IgM negative IgM | |
| Hepatitis B test | | Negative IgG and IgM negative IgM | |
| Hepatitis C test | | negative | |
| HIV test | | negative | |
| Ova and parasite examination | | | negative |
| Complete blood count | negative | | |
| Echocardiogram | | Normal | |

Hb: hemoglobin; Ht: hematocrit; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; LDH: lactate dehydrogenase; HIV: human immunodeficiency virus

39º to 40.5º C for 25 days, unexplained loss of 2kg, night sweats and cough. He did not report any gastrointestinal symptoms or pain. Five days before the beginning of intermittent fever, he had his hand cut by a kite line coated with powdered glass, which resulted in an edema that resolved spontaneously.

Initial physical examination did not reveal any abnormalities. The patient had the results of tests requested a few days before, during an outpatient consultation: normal chest X-ray, negative PPD skin test, leukocytosis and elevated C-reactive protein in CBC (Table 1).

In the emergency department, the workup for fever of unknown origin included echocardiogram and abdominal ultrasound focused on the investigation of possible infections, rheumatologic and oncologic etiologies (Table 1).

Abdominal US revealed a relatively well-defined heterogeneous nodular mass measuring 5.5 x 7.0 cm, compatible with liver abscess. He was hospitalized and received IV metronidazole, oxacillin and amikacin. On the second hospitalization day, the pediatric surgery team requested an abdominal CT to plan the operation (Figure 1).

Because of the abscess size, the patient underwent open surgical drainage with placement of a Watterman drain. The culture of drained material showed growth of methicillin-sensitive *Staphylococcus aureus*. Treatment continued for four weeks with oxacillin, whereas all the other antibiotics were discontinued.

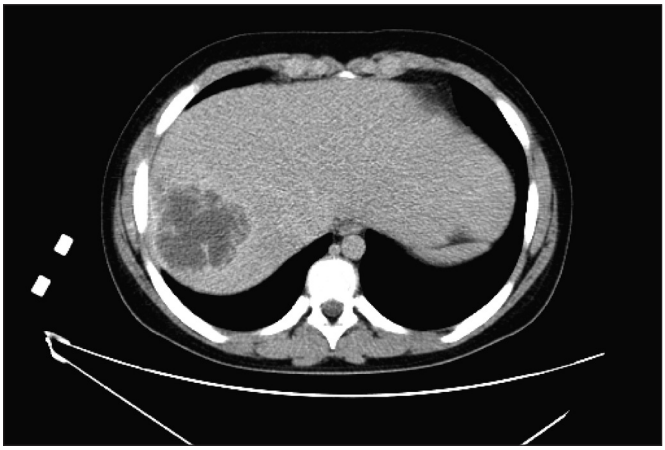

**Figure 1 -** Abdominal CT scan shows hypoechoic heterogeneous lesion with irregular margins and areas of increased density, measuring 9.5 x 7.3cm, in segment VII

## Discussion

The case reported here is an example of a pathology not usually found in the literature, but extremely important due to its high morbidity and mortality[3,4] and the worldwide differences in its epidemiology. According to studies in developed countries, the signs and symptoms with which our patient presented were not enough to suggest the presence of a liver abscess, but studies conducted in developing

countries demonstrated that findings in the patient's history suggested that diagnosis.

A fever of unknown origin is a common finding in pediatric clinical routine, and liver abscesses should be included in the differential diagnosis. In general, symptoms are clearer and include abdominal pain, anorexia, nausea and vomits associated with fever[3,4,9,12]. In the case described here, the patient had a few unspecific symptoms, including prolonged fever and weight loss, without any gastrointestinal changes, which contributed to the delay in diagnosis.

Our patient did not have the diseases associated with liver abscess, according to studies in developed countries[1,2,5], such as liver transplant, diabetes mellitus, cancer, biliary pathologies and chronic granulomatous disease, which also made diagnosis difficult initially.

In contrast, according to studies conducted in developing countries, such as Brazil[8] , China[13] and India[14], the patient had relevant risk factors. Some studies, such as the one conducted by Ferreira *et al*, published in 1997, suggested that a relevant predisposing factor is a history of skin lesions, which may be found in up to 35% of the cases[8]. As described above, this type of association was found in our patient, who had hurt his hand a few days before the onset of fever.

Another factors that differs in the literature of developed and developing countries is the frequent association of liver abscess with helminth infection[8,9,13,15], which may justify the substantial difference in the occurrence of liver abscess in these two groups of countries. A Brazilian study of eight cases of liver abscess in children, published in 1995, reported that three of them, that is, 37.5% of the cases, had *Ascaris lumbricoides* infection, which may have been a predisposing factor for the development of the liver abscess[15]. Another study, conducted by Ferreira *et al* in 1997 examined 65 children with a diagnosis of liver abscess; results of fecal examination, available for 36 of them, revealed helminth infection in 80.6% of the cases under analysis[8]. Similarly, a study conducted in India in 1998 found infection by *Ascaris lumbricoides* in 38.9% of the children with a diagnosis of pyogenic liver abscess[14].

In helminth infection, particularly when there is passage of larvae through the hepatic tissue, there might be immunomodulation characterized by eosinophilia, increased IgE production and stimulation of T2 response in association with T1 suppression, which favors the formation of granulomas and increases the susceptibility to bacterial infections[8,9,16,17]. In addition to that, the presence of parasites in the biliary duct leads to biliary stasis, which also favors secondary bacterial infections[18,19].

*Staphylococcus aureus* was the etiologic agent detected in the material drained from the patient. The literature in both developing and developed countries shows that this is the main etiologic agent of liver abscesses in pediatric populations[8,20].

Mechanisms previously described explain why the incidence of liver abscess is higher in developing countries, as hygiene and sanitation are, in general, not adequate, which promotes the occurrence of parasitoses.

This case report demonstrated that pediatricians should be aware of the common causes of fevers of unknown origin, know how to develop a systematic diagnostic approach, and, when a liver abscess is diagnosed, investigate whether *Staphylococcus aureus* is the etiologic agent, especially when there is a history of skin rupture. This case also demonstrated the importance of referring not only to the literature produced in developed countries, but also to the studies conducted in developing countries because of the different socioeconomic realities that may lead to very different environments, a factor that should also guide clinical thinking.

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