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Case Report

Pyogenic liver abscess in a child with concomitant infections – *Staphylococcus aureus*, *Echinococcus multilocularis* and *Mycobacterium tuberculosis*

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Summary

Pyogenic liver abscess is an uncommon but important and potentially life-threatening disease that occurs whenever there is failure of clearance of an infection in the liver. Work presents a rare case of pyogenic liver abscess with confirmed bacterial aetiology of *Staphylococcus aureus*, subsequently confirmed *Echinococcus multilocularis* and suspected *Mycobacterium tuberculosis* liver infection in 6 years old child. Moreover, several other parasitic diseases were recorded. According to clinical presentation of diseases, it could be supposed that liver impairment caused by alveolar echinococcosis and potentially also by *M. tuberculosis* could be the predisposition site for the capture of *Staphylococcus aureus* in altered liver tissues during its haematogenous spreading, and thus contributed to the development and subsequent clinical presentation of pyogenic liver abscess. The presence of three different aetiological agents complicated the diagnostic process as well as the therapy of the patient and made her prognosis uncertain. Proper diagnosis of multiloculated liver abscesses, with echinococcosis and hepatic tuberculosis considered in the differential diagnosis, is therefore crucial to administration of early and appropriate treatment.

Keywords: Pyogenic liver abscess; *Staphylococcus aureus*; *Echinococcus multilocularis; Mycobacterium tuberculosis*

Introduction

Pyogenic liver abscess is an uncommon but important and potentially life-threatening disease. The two major mechanisms for the development of pyogenic liver abscesses are local spread from contiguous infections within the biliary tree or peritoneal cavity, and haematogenous seeding. When the biliary tree is the source of infection enteric gram negative aerobic bacilli, *Enterococci*, *Escherichia coli* and *Klebsiella* spp. are reported as frequently isolated (Rahimian *et al*., 2004; Chen *et al*., 2014; Moore *et al*., 2014). *Staphylococcus aureus* and *Streptococcus* spp. are the most common causes connected with the haematogenous spread (Jha *et al*., 2007).

Alveolar echinococcosis (AE) is one of the most serious helminthic diseases of men. Humans acquire infection after the accidental ingestion of *E. multilocularis* eggs and subsequently larval stages proliferate primarily in the liver, but can also spread into extrahepatic structures and even metastasize to other organs. The clinical diagnosis is based on clinical findings, lesion morphology shown by imaging techniques, serology, histopathology and molecular nucleic acid detection (Naik *et al*., 2015; Szilágyová *et al*., 2015). Untreated disease is usually considered lethal, as no curative treatment is available, except surgical resection of metacestode in an early stage of disease (Kern *et al*., 2006). Long-term drug treatment with benzimidazoles is mandatory in all patients; temporarily after complete lesions resection and for life in all other cases (Kern *et al.,* 2010).

Table 1. Trends of laboratory tests results

PARAMETER	Refer. values	Day 1	Day 3	Day 7	Day 11	Day 14	Day 21
Leukocytes (per mm^3)	4.5 – 13	20.53	40.85	37.89	35.82	13.09	14.21
Neutrophils (per mm^3)	1.8 – 7.0	14.74	32.05	30.17	27.27	9.65	7.47
Haemoglobin (g/l)	118 – 150	104	106	81	80	105	102
Platelets (per mm^3)	150 – 440	248	450	844	1250	998	723
C-reactive protein (mg/l)	< 5	169.9	133.9	215.7	118.9	71.8	22.3
Gama glutamine transferase (µkat/l)	0.08 – 0.4	1.0	1.24	3.44	6.09	–	4.95
Alanine aminotransferase (µkat/l)	0.05 – 0.78	1.25	0.73	0.41	0.28	–	0.21
Albumin (g/l)	35 – 53	27.9	28.7	30.3	35.5	–	–
Procalcitonin (µg/l)	< 0.5	–	–	3.25	6.69	0.789	0.12

Isolated tubercular abscess of liver is a very rare form of extrapulmonary tuberculosis (TB). The most of cases are usually clinically silent and therefore possibly under-diagnosed and under-reported in clinical practice (Wu *et al*., 2013). Tuberculous bacilli can reach the liver via haematogenous dissemination, generally from the lungs, or by local spread from the gastrointestinal tract. The diagnosis is usually difficult to confirm and is frequently confused with pyogenic or amoebic liver abscess (Chien *et al*., 1995; WHO, 2015).

The work presents a rare case of pyogenic liver abscess with confirmed bacterial aetiological agent *Staphylococcus aureus*, subsequently confirmed *Echinococcus multilocularis* and suspected *Mycobacterium tuberculosis* liver infection in 6 years old child.

Case report

A 6-year-old girl was presented with a history of fever, diarrhoea and vomiting in August 2013. Patient belonged to Roma ethnic minority and came from family living in poor socio-economic conditions. Her parents, legal representatives, agreed with all investigations and signed the informed consent prior to medical examinations and hospitalisations.

The medical history of patient was unremarkable. She received Calmette-Guérin bacilllus vaccine at birth. Laboratory blood examination revealed elevated C-reactive protein (CRP) and an abdominal ultrasound (USG) showed the presence of numerous hypoechogenic lesions in the liver, hepatosplenomegaly and as-

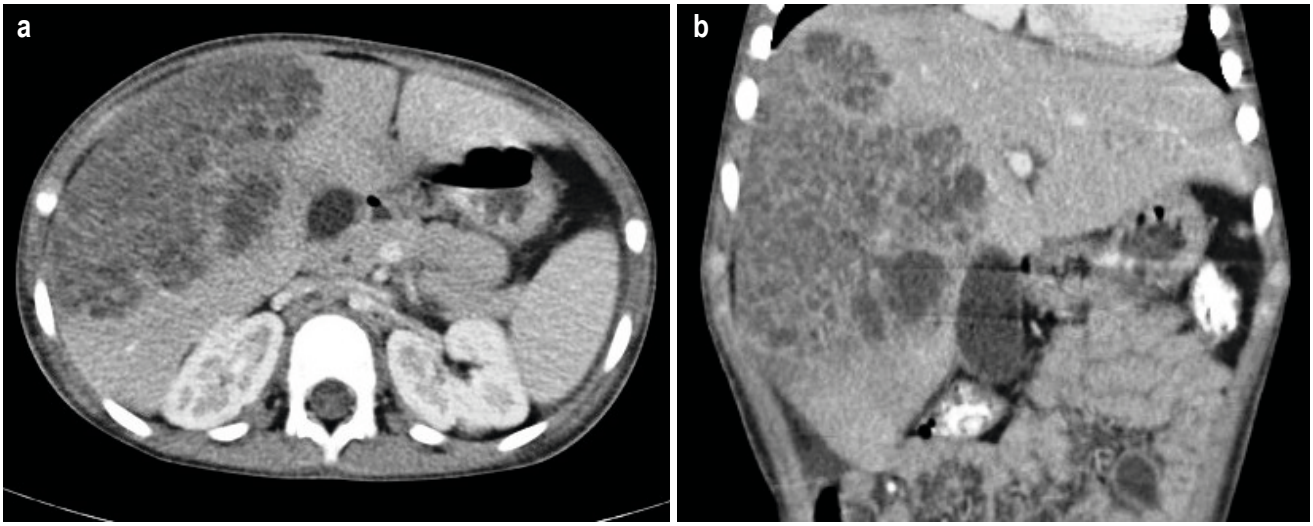

Fig. 1. CT images revealed hepatomegaly (up to 16 cm) with large non-homogenous, hypodense lobulated lesions in all right liver lobe segments and in S1 and S4 segments. Axial view (a) and coronal view (b).

cites. The physical examination revealed abdominal distension, non-tender to palpation and hepatomegaly with a liver edge palpable in inguinal region. The results of some laboratory blood tests are shown in Table 1. Bilirubin, electrolytes, blood urea, nitrogen and creatinine were within the physiological range. A computed tomography (CT) scan confirmed hepatomegaly (up to 16 cm) with large non-homogenous, hypodense lobulated lesions observed in all right liver lobe segments and also in S1 and S4 segments (Fig. 1). The presumptive diagnosis was parasitic liver abscess or tumour, such as hemangioendothelioma.

The treatment began with an empiric antibacterial therapy and mebendazole. Later, serological and parasitological examinations showed the positivity to several bacterial and parasitic pathogens. Tests aimed to detect *Mycobacterium tuberculosis* infection did not confirm tuberculosis at the beginning (Table 2). The levels of oncomarkers were within reference values and immunological tests excluded primary and secondary immunodeficiency.

As the progression of hepatic lesions on USG was observed on day 10, open liver biopsy was performed. During biopsy numerous whity solid lesions, with 2 – 3 cm in diameter and necrosis in the center, in the liver parenchyma were observed. Histological examination of liver parenchyma revealed the presence of numerous abscesses and the absence tumorous lesions. The culture from surgery grew *Staphylococcus aureus*; therefore the antibiotic treatment was changed to linezolid.

PCR amplifications of *E. multilocularis* mitochondrial NAD1 and NAD2 genes and subsequent sequencing confirmed the presence of *E. multilocularis* DNA in the liver tissue sample (Table 2). Control CT examination did not confirm the presence of *E. multilocularis* lesions in lungs and brain.

On day 22 patient´s clinical status gradually improved, the fever disappeared, CRP decreased and USG showed the reduction of liver lesions. The presence of *Mycobacterium tuberculosis* DNA in liver tissue sample was confirmed afterward (Table 2), but the results of several examinations aimed to confirm the diagnosis of tuberculosis were negative (microscopic and cultivation of gastric aspirates and laryngeal specimen, SPOT assay). CT scan confirmed parahilous lesion in lungs and repeated CT liver scan demonstrated marked regression of lesions. Because of probable diagnosis of tuberculosis the combined antitubercular therapy was applied for six months.

In March 2015 the patient was checked up and an ultrasound examination showed only discretely irregularly mixed echogenicity of liver parenchyma (Fig. 2).

Table 2. Results of serological and parasitological examinations

EXAMINATION	PARAMETER / TEST	RESULT
PARASITOLOGICAL	*E. multilocularis* PCR (liver sample)	**POSITIVE**
	E. granulosus IgG antibodies	Negative
	E. multilocularis IgG antibodies	Negative
	Toxocara IgG antibodies	**POSITIVE**
	Toxoplasma IgG antibodies	**POSITIVE**
	Parasitological stool examination	***Ascaris lumbricoides*** ***Trichuris trichiura***
BACTERIOLOGICAL	Microbiological cultivation (liver sample)	***Staphylococcus aureus***
	Mycobacterium tuberculosis PCR (liver sample)	**POSITIVE**
	Mycobacterium tuberculosis Tests (Quantiferon test; Tuberculin Skin test; Microscopy and cultivation for Acid-fast bacilli from respiratory and gastric aspirates; SPOT assay)	Negative
	Yersinia enterocolitica	Negative
	Hemo-culture*	***Stenotrophomonas maltophilia****
VIROLOGICAL	Cytomegalovirus	Negative
	HIV test	Negative
	Viral hepatitis	Negative
	Epstein-Barr virus	Negative
FUNGAL	*Candida* mannan antigen	**POSITIVE**

**S. maltophilia* detected on day 12; former hemo-cultures were negative

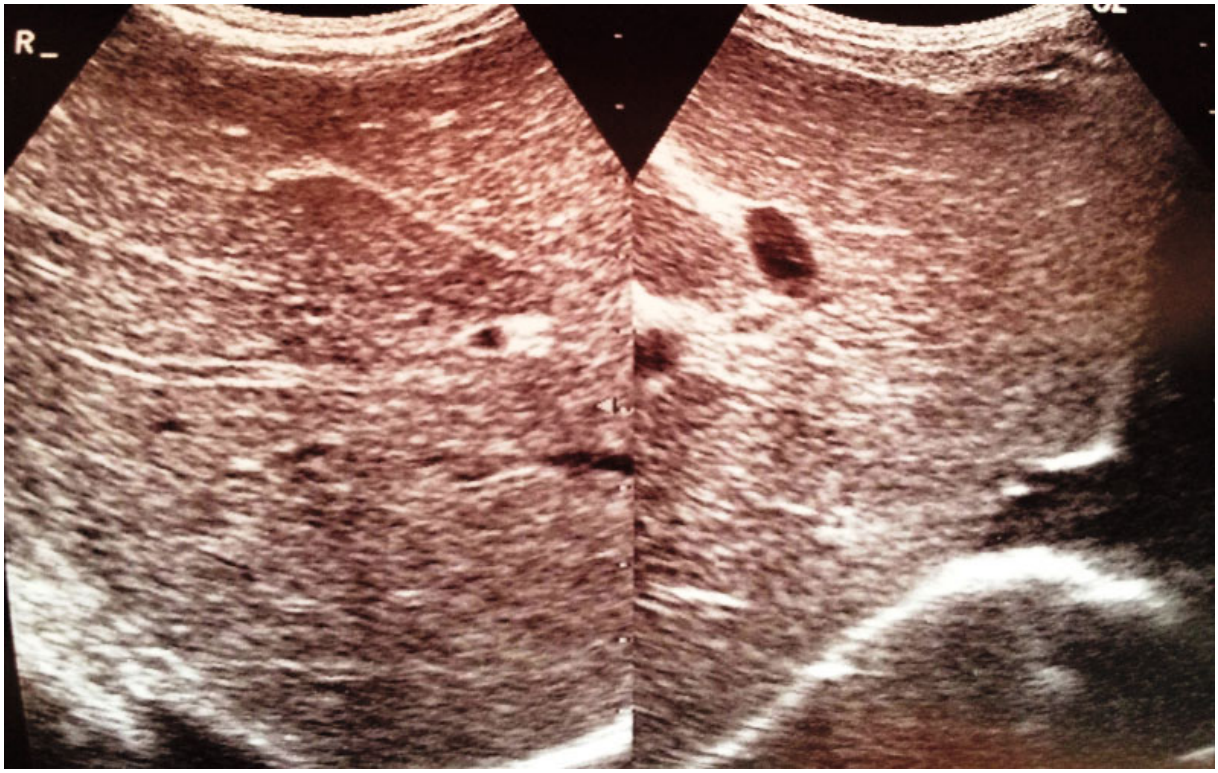

Fig. 2. Ultrasound of the liver during the last control of the patient confirmed almost physiological findings with discretely irregularly mixed echogenicity of right liver lobe parenchyma

Discussion

In presented patient, microbiological cultivation from the material obtained during the surgery revealed *Staphylococcus aureus* as the underlying aetiology of liver abscess formation. Later, the presence of *Mycobacterium tuberculosis* and *Echinococcus multilocularis* DNA in liver tissue samples were confirmed.

Pyogenic liver abscess, considered a potentially fatal disorder, occurs whenever there is failure of clearance of an infection in the liver. The most commonly identified causative organisms are anaerobes and aerobic gram-negative rods, but *Staphylococcus aureus*, detected also in presented patient, is also common. Primary liver tuberculosis is a rare form of extra-pulmonary TB and only few cases have been reported worldwide. The clinical presentation of hepatic TB is usually non-specific. High-grade fever, upper abdominal pain, weight loss and hepatomegaly are the most frequently observed clinical findings (Mourad *et al*., 2014; Carrara *et al*., 2015). Diagnosis of liver tuberculosis in our patient was confirmed only by PCR from liver tissue specimen, while results of respiratory and gastric aspirates microscopy, tuberculin skin test and Quantiferon test were negative. Therefore the patient could be considered only as probable case of tuberculosis. On the other hand, according to some authors (Elias *et al.,* 2001; Yang *et al*., 2009) the results of tuberculin tests can be negative in patients with helminth infections due to the switch of Th1 immune response to Th2 response. Such phenomenon was recorded in two patients with simultaneous tuberculosis and echinococcosis in China (Yang *et al*., 2009). Similarly, Elias *et al*. (2001) reported worse response to tuberculin skin testing in helminth infected Ethiopian immigrants than in immigrants who had been dewormed. The evidence about the inhibitory effect of *Onchocerca volvulus* infection on the immune response to *M. tuberculosis* and *M. leprae* infection in children was also published (Stewart *et al*., 1999). Therefore we may suppose that in our patient, multiple helminth infections could contribute to negativity of tuberculin skin test.

The third severe diagnosis of patient was alveolar echinococcosis. The most frequent AE morphological profile is characterised by intrahepatic heterogeneous, infiltrative mass with irregular outlines and necrotic center that appears on USG as hypoechoic and hyperechoic lesions (Reuter *et al*., 2001). In our case the confirmation of the diagnosis was complicated by concomitant liver infections and negative results of serological examinations. Pathological liver findings on CT and USG were predominantly caused by *S. aureus*; therefore it was almost impossible to distinguish the real extent of changes caused by tapeworm metacestode. Moreover, significant regression of liver lesions observed in patient suggests some resistance to disease. Although spontaneous death of metacestodes has been described in some cases (Gottstein *et al*., 2001), the most of them should be classified as possible AE cases. Even the lack of metabolic activity detected by imaging techniques does not mean the parasite death and indicates only the suppression of periparasitic inflammatory activity (Kern *et al*., 2010; Reuter *et al*.,

2008). Except three aforementioned diagnoses, positivity to several other pathological agents was documented, namely *Ascaris lumbricoides* and *Trichuris trichiura* and seropositivity to *Toxocara* spp., *Toxoplasma gondii* and *Candida mannan* antigen. Finally, after the long-term treatment with different drug combinations the patient clinical status improved and in March 2015 the ultrasound confirmed only discrete findings of irregularly mixed echogenicity of liver parenchyma at the site of the previous liver lesions.

Concomitant or mixed infection is the situation in which two or more genetically different infectious agents coexist in the same host and can cause a numbers of different interactions between each other. Records on the effects of bacterial infections on helminths are usually indirect; and it seems that helminth infections more often influence the course of parallel bacterial disease (Cox, 2001). Presented patient came from the family with poor socio-economical conditions and lived in segregated Roma settlement. Parasitic infections are very frequent in Roma settlements (Rudohradská *et al.,* 2012); therefore we can suppose the positivity of our patient to parasites from her early childhood or even the possibility of reinfections. Moreover, later diagnosed alveolar echinococcosis is known to have slow progress and very long incubation period. Therefore, liver impairment that had been caused by AE and/or by *M. tuberculosis* could be the predisposition site for the capture of *Staphylococcus aureus* in altered liver tissues during its haematogenous spreading. According to the characteristic clinical course of mentioned separate diseases, we suppose that the presence of clinically silent alveolar echinococcosis and probably also of liver focal tuberculosis was revealed within the diagnostic process of pyogenic liver abscess.

We can conclude that proper diagnosis of multiloculated liver abscesses, with echinococcosis and hepatic tuberculosis considered in the differential diagnosis, is crucial to administration of early and correct treatment.

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