

A case of acalculous cholecystitis in the course of dengue fever in a traveller returned from Brazil

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ABSTRACT

Background: Dengue is the second cause of fever after malaria in travellers returning from the tropics. The infection may be asymptomatic or it may manifest itself with fever only, some patients, however, may develop haemorrhagic symptoms and shock.

Materials and methods: A 58-year-old woman came to the University Centre of Tropical Medicine in Gdynia after returning from a tourist journey to Brazil because of fever up to 39°C and malaise. She had lived in South America many years and then moved to Europe 3 years before hospitalisation. On admission physical examination revealed fever, dry mucosa, moderate hypotension and tachycardia. In the laboratory test results, leukopenia, thrombocytopenia and elevated transaminases were observed. On the second day of the hospitalisation, the patient reported epigastric pain, clinical examination revealed tenderness of the abdomen and macular rash on the skin of the trunk and thighs. The ultrasonography revealed an enlarged gallbladder with thickened walls, with hypoechogenic area surrounding it, a dilated common biliary duct of heterogenic echo, and some free fluid in the peritoneal cavity. An exploratory laparotomy was performed after 24 h because of the persisting strong abdominal pain and high fever. Intraoperatively, enlarged mesenteric lymph nodes were found, with no symptoms of gallbladder pathology. The postoperative course was uncomplicated and the positive result of immunochromatographic assay for dengue was obtained.

Results: The acalculous cholecystitis has been described in the course of various diseases and conditions. The typical symptoms include pain in the right hypochondriac region, fever, positive Murphy's sign, and abnormal liver function tests, which were observed in the presented case. Cholecystectomy is not usually indicated in the course of dengue (typically a self-limiting disease) due to a high risk of bleeding.

Conclusions: The case provides a rationale for the inclusion of acalculous cholecystitis in the differential diagnosis in patients with abdominal pain returning from dengue endemic areas.

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Key words: acalculous cholecystitis, dengue

INTRODUCTION

Dengue is an infectious disease caused by the dengue virus (DENV) of the *Flaviviridae* family. It is endemic in the tropical and subtropical zones. The vector for the virus is the mosquito of the *Aedes* genus. Fifty to 100 million people are affected yearly by the disease [1–3] and 50,000 (1%)

require hospitalisation [1]. The disease has been limited to tropical areas; however, there have been recent reports of endemic cases in France and Croatia [4, 5]. According to the serologic findings, dengue is the cause of 3–8% fever cases in travellers returning from the tropical zones [1]. Dengue is the second cause of fever after malaria in

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travellers returning from the tropics. The symptoms of the disease may vary widely: the infection may be asymptomatic or it may manifest itself with fever only whereas some patients develop haemorrhagic symptoms and shock. The number of dengue cases has increased 30 times in the last four decades and the geographic range of the disease has also extended.

The four serotypes of dengue virus are distinguished: DENV1, DENV2, DENV3, and DENV4. Infection with one of the serotypes results in long-lasting/lifetime immunity against this serotype, but does not protect against infection with other serotypes, and may even contribute to the more severe course of the disease in the case of a reinfection.

CASE REPORT

A 58-year-old woman, citizen of Sweden, was admitted to the University Centre of Tropical Medicine in Gdynia after returning from a 2-week long tourist journey to Brazil because of fever up to 39°C and malaise. The patient returned to Poland 2 weeks before admittance to the hospital. The woman had lived in South America for many years and then moved to Europe 3 years before hospitalisation. She had no history of chronic diseases.

The laboratory tests performed in the outpatient clinic revealed leukopenia (2.2 G/L) and thrombocytopenia (89 G/L).

The physical examination on admission revealed the body temperature 39°C, dry mucosa, arterial blood pressure of 100/65 mm Hg, heart rate 112/min. The patient was very weak. The general status was described as moderate-severe. Abnormal laboratory tests results are presented in the Table 1.

Moreover, (1) In the urine analysis, the following abnormalities were present: protein (+), glucose (++), erythrocytes 2 in the field of view (FOV), leukocytes 5 in the FOV, small number of bacteria; (2) Abdominal ultrasonography revealed: slightly enlarged liver, thickened walls of the gallbladder with visible echogenic area as in an inflammatory reaction, the common bile duct was 8 mm wide with linear hyperechogenicity, and small amount of free fluid was present perihepatically and in the small pelvis.

Intravenous fluids and antipyretics were administered. On the second day of hospitalisation, the patient reported epigastric pain; the clinical examination revealed tenderness of the whole abdomen, with no rebound tenderness or abdominal guarding, the Murphy's sign was negative. Moreover, macular rash developed on the skin of the trunk and thighs. Complete blood count revealed further decrease in the number of thrombocytes. Malaria was excluded with the peripheral blood smear and the fast immunochromatographic assay, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections were also ruled out. Blood and faeces

Table 1. The abnormal laboratory findings at admittance to the Department of Tropical and Parasitic Diseases

Marker [Unit]	Result	Norm
White blood cell count [G/L]	1.6	4–10
Thrombocytes [G/L]	47	140–440
Glutamic oxaloacetic transaminase [U/L]	235	5–41
Glutamic pyruvic transferase [U/L]	522	5–37
Gamma-glutamyl transferase [U/L]	155	< 71
D-dimer [ng/mL]	5434	< 500
Activated partial thromboplastin time [s]	42	24–35
Fibrinogen [g/L]	1.65	2–4
Total protein [g/L]	55.3	64–83
Albumins [%]	56–66	50
Gamma-globulins [%]	25	11.1–18.8
C-reactive protein [mg/L]	32	< 5

cultures, faeces examination for parasitic diseases were negative, *Streptococcus salivarius* was cultured in the urine. Fever up to 39.2°C persisted in the patient.

Along with the decrease in the blood platelet count, the elevated activity of glutamic oxaloacetic transaminase (GOT, aspartate transaminase) 927 U/L, glutamic pyruvic transferase (GPT, alanine transaminase) 1793 U/L, gamma-glutamyl transferase (GGT) 1086 U/L, alkaline phosphatase (ALP) 522 U/L was observed in laboratory tests. The repeated abdominal ultrasonography revealed gallbladder sized 56 × 29 mm with thickened walls, with hypoechogenic area surrounding it, the common biliary duct of heterogenic echo, 7 mm in diameter, and the free fluid was present between the intestinal loops in the lesser pelvis. The blood sample was sent to an external laboratory (the Department of Tropical and Parasitic Diseases, Medical University of Poznan) for serologic testing for dengue. Intravenous amoxicillin/clavulanic acid and metronidazole were administered. After surgical consultation, the patient was referred to a surgical department for observation, where exploratory laparotomy was performed after 24 h because of persisting strong abdominal pain and high fever. Intraoperatively, enlarged mesenteric lymph nodes were found, with no symptoms of gallbladder pathology. The histopathologic examination of a lymph node revealed reactive lymphadenitis, while histopathologic appearance of a liver fragment was suggestive of toxic injury.

The postoperative course was uncomplicated and the wound was healing by first intention. On the third day after the operation, the patient was transferred back to our department. Meanwhile, the result of immunochromatographic

assay for dengue was obtained: a high-positive band for specific IgM antibodies and low-positive band for specific IgG antibodies were present, which corresponded to the secondary dengue infection. Other laboratory tests came back to normal values, apart from high GGT activity (315 U/L), D-dimer concentration (2005 ng/mL) and serum protein electrophoresis abnormalities. The clinical condition of the patient improved and laboratory results were within normal range throughout further outpatient observation.

DISCUSSION

The four clinical courses of dengue virus infection have been distinguished by the World Health Organisation (WHO) classification, which was developed 30 years ago, based on observations of patients in paediatric departments in Thailand. Recently, however, the course of the disease has changed, especially in the region of Latin America and the Caribbean [6]. The “classical” WHO classification does not include atypical forms of the disease: encephalopathy, meningitis, encephalitis, polyneuropathy, Guillain-Barre syndrome, hepatitis including its fulminant form, myocarditis, acalculous cholecystitis, acute pancreatitis, peritonitis, rhabdomyolysis, pulmonary haemorrhage, acute respiratory distress syndrome (ARDS), acute renal failure, haemolytic-uremic syndrome, disseminated intravascular coagulation (DIC) [6]. The unusual manifestations of dengue are present in up to 15.8% of patients [7].

The course of the disease depends on the serotype of the dengue virus. Neurological disorders have been associated with the serotypes DENV2 and DENV3 while the gastrointestinal and other atypical forms have been linked to the infection with serotype DENV2. The serotype DENV2 is the most frequently diagnosed serotype in secondary infections in both Americas. In the presented case, both the epidemiological data (repeated travel to Brazil) as well as the clinical picture indicate infection with the serotype DENV2.

The acalculous cholecystitis has been described in the course of various diseases and conditions including trauma, vasculitis, parenteral alimentation, mechanical ventilation, salmonellosis, staphylococcal infections, brucellosis, leptospirosis, rickettsiosis or cytomegaly [6, 8–14]. The thickening of gallbladder wall is the most frequent (43–59%) ultrasonographic finding in patients with dengue fever [15, 16] whereas in the case of dengue haemorrhagic fever it may be found in up to 90% of patients [17–20]. The condition occurs in 7.6% to 38% of patients [9, 21, 22]. Typical symptoms include pain in the right hypochondriac region, fever, positive Murphy’s sign, and abnormal liver function tests [6, 9], which were observed in the presented case. A significant correlation between gallbladder wall thickening and the course of the disease (including progression to dengue haemorrhagic fever) has been demonstrated [6].

Usually, the thickness of gallbladder wall in dengue patients exceeds 3 mm in ultrasonography, while thickness exceeding 5 mm indicates a severe course of the disease [23].

Acalculous cholecystitis should be suspected in patients infected with dengue reporting abdominal pain. The sonographic examination in these patients may reveal free fluid around the gallbladder, sonographic Murphy’s sign, striating of gallbladder wall indicating its oedema, presence of intraparietal gas, and mucosal sloughing.

Acalculous cholecystitis constitutes 10–15% of all cholecystitis cases of various aetiology and 40% of cases are complicated by a gallbladder perforation [8]. The mortality in acute acalculous cholecystitis accompanying various diseases may reach 50%. Rapid progression to gangrene and gallbladder wall perforation have been described, therefore, strict observation of the patient and prompt surgical intervention are warranted [24].

Acalculous cholecystitis in the course of dengue is usually a self-limiting disease and the thickness of gallbladder wall returns to normal after recovery. Cholecystectomy is usually not indicated in these patients due to a high risk of bleeding [25]. However, it may be mandatory if gangrene, gallbladder wall perforation or diffuse peritonitis is suspected.

The presentation and course of the illness in this patient corresponded to acute acalculous cholecystitis. Since rapid serologic tests for dengue were unavailable during the patient’s hospitalisation, her clinical condition did not improve and laboratory parameters gave evidence of liver injury and cholestasis, the patient was treated surgically. Explorative laparotomy was performed; however, there were no indications for cholecystectomy.

CONCLUSIONS

The presented case provides a rationale for the inclusion of acalculous cholecystitis in the differential diagnosis of abdominal pain in patients returned from dengue endemic areas. In such cases, strict surgical observation is warranted.

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