

Abdominal pain in a patient with recurrent malaria – a case report

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Currently the majority of malaria cases in Europe are imported by international travellers and immigrants. Typical clinical signs of malaria are recurrent fever, hepatosplenomegaly and haemolytic anaemia. Abdominal pain is not a specific clinical sign of malaria. We present a clinical case of three-day malaria in a 17-year-old Indian citizen who was admitted to the Ternopil Regional Children's Hospital with fever and severe abdominal pain. The peculiarity of this case was the presence of fever and severe abdominal pain at the onset of the disease, which led to admission of the patient to surgical department and delayed correct diagnosis. Careful, thorough case history is one of the key points on the way to the accurate diagnosis. There is a need to increase the physicians' awareness of malaria in patients with abdominal pain who have come from malaria endemic countries.

Key words: MALARIA; ABDOMINAL PAIN; DIAGNOSIS

INTRODUCTION

Malaria is a life-threatening disease caused by parasites that are transmitted to people through bites of infected female Anopheles mosquitoes (1). There are four species of human malaria parasites: three-day malaria, *Plasmodium (P.) vivax*; four-day malaria, *Plasmodium (P.) malariae*; a special species of three-day malaria, *Plasmodium (P.) ovale*; and tropical *Plasmodium (P.) falciparum* (1,2). Globally, malaria remains a big problem in the world. According to the World Health Organisation (WHO), in 2017 about 219 million malaria cases and 435,000 related deaths were estimated worldwide (2).

Currently, more than 99% of malaria cases in Europe are imported by international travellers and immigrants (3,4); about 6-8 thousand malaria cases are reported annually in Europe (2, 4). In 2015, WHO declared that the European region was the first in the world to eliminate malaria, although climatic conditions of southern Europe are still favourable for mosquito genus Anopheles and parasite development (1). About 50 cases of malaria and the single related deaths are reported annually in Ukraine; 80% of the cases are caused by *P. falciparum* (5).

Typical clinical signs of malaria are recurrent fever, hepatosplenomegaly and haemolytic anaemia (1, 5). Characteristic symptoms of *P. vivax* malaria are tertian fever and severe chills (6). A study showed that not all cases of three-day malaria

demonstrated a classical cyclic fever pattern (6). The prevalence of abdominal pain in malaria, according to that study, ranges from 21.4% to 29.5% (6). Abdominal pain is mostly associated with *P. falciparum* malaria (7). The duration of the existence of plasmodia in the human body (without treatment) is up to 1.5 years for *P. falciparum*, up to 4 years for *P. vivax* and *P. ovale*, and in some cases for *P. malariae* for life. After a short stay in the blood, the malarial plasmodium sporozoites penetrate the hepatocytes of the liver, thereby giving rise to the preclinical hepatic (exoerythrocytic) stage of the disease. In the process of asexual reproduction called schizogony, from one former sporozoite, which turns into a schizont in the liver cell, 2,000 to 40,000 hepatic merozoites are formed. In most cases, these daughter merozoites enter the bloodstream again after 1-6 weeks (8).

The disease can become symptomatic after a long incubation period or from relapse, even up to several months after returning from an endemic area (5, 9).

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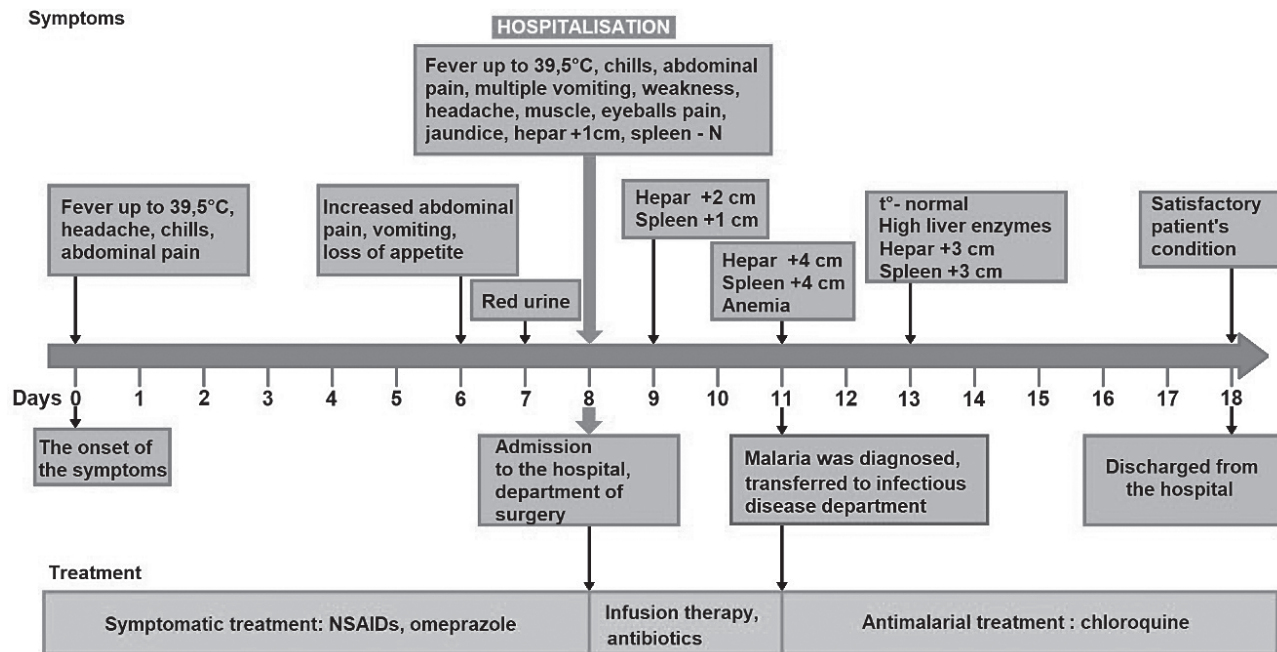


FIGURE 1. Timeline of symptoms in our patient with malaria.

CASE REPORT

We present a clinical case of three-day malaria in a 17-year-old Indian citizen who was admitted to the Ternopil Regional Children's Hospital with fever and severe abdominal pain. The patient was a first-year student at Ternopil University. The patient complained of severe abdominal pain, more pronounced in the right iliac region, recurrent vomiting, general weakness, fever up to 39-39.5 °C, severe headache, muscle pain, eyeball pain, chills, and red colour of urine. A timeline of symptoms is presented in Figure 1.

The first symptoms were noted eight days before admission and included fever up to 39-39.5 °C, which was accompanied by headache, chills, and moderate abdominal pain. A slight improvement was observed after intake of the non-steroidal anti-inflammatory drug (NSAID). Abdominal pain increased two days before admission, localized more in the right iliac and umbilical areas and accompanied by vomiting, chills, and loss of appetite. A day before admission, urine became red. The patient did not seek medical advice, he was taking omeprazole and NSAID, with slight improvement. As the condition of the patient did not improve during the week, an ambulance was called. At admission, the patient did not report any previous diseases.

Clinical examination revealed severe general condition of the patient. The patient was conscious. Fever 38.5 °C, mild jaundice, and tachycardia (96/min) were revealed during the examination. The abdomen was painful on palpation, especially in the right iliac region, muscular defense was also detected

in this region. Symptoms of peritoneal irritation were doubtful. The liver was slightly enlarged (+1 cm), and the edge of the spleen was palpated. Pasternatsky's symptom was weakly positive on both sides. Diuresis was sufficient. On the day of admission, urine was cloudy and red.

Taking into account pronounced abdominal pain, painful abdomen and muscular defense in the right iliac region, symptoms of peritoneal irritation and fever, acute appendicitis was suspected and the patient was hospitalized in the surgical department. At admission, complete blood count was without significant changes (only 9% of stab leukocytes). The dynamic observation was conducted, and infusion therapy of saline and 5% glucose solution was prescribed.

On the morning of the next day, the patient's general condition improved. Body temperature returned to normal. The patient complained of headaches and eye pain. Pain in the right iliac region was reduced. Vomiting did not recur. Deep palpation of the abdomen detected slight tenderness in the right iliac and umbilical areas. Symptoms of peritoneal irritation were not detected. The peristalsis was satisfactory. However, clear signs of hepatosplenomegaly were noted, i.e., enlarged liver (2 cm protruded from the edge of the right costal arch), the spleen 1 cm protruded from the edge of the left costal arch.

Biochemical blood testing revealed hyperbilirubinemia (57.6 mmol/L), hypoproteinaemia (52.0 g/L), high level of aspartate aminotransferase (78.4 IU/L), slightly increased level of alanine aminotransferase (50.4 IU/L), and increased

level of urea (9.6 mmol/L). Ultrasound investigation of internal organs confirmed liver and spleen enlargement, along with an enlarged pancreas. Esophagogastroscoy revealed gastropathy and duodenal-gastric reflux. Acute appendicitis was ruled out by ultrasound examination and improvement of the clinical picture.

Around noon, the patient's condition worsened again, temperature increased, also with headache, eye pain and abdominal pain. Acute nonspecific mesenteric adenitis was suspected. Antibacterial therapy (ceftriaxone) was prescribed. Body temperature increased from normal (36.4 °C) to hectic (40.4 °C) during the day.

Additionally, it was established that two years before, the patient had been treated for malaria in India and had not received anti-relapse therapy. Microscopy of thin blood film for malaria plasmodium detected *P. vivax*.

The patient was transferred to the infectious disease department and antimalarial treatment (chloroquine) was prescribed. As a result of treatment, the patient's condition improved. Body temperature normalized on the second day of specific treatment. However, thrombocytopenia ($107 \times 10^9/L$), leukopenia ($2.9 \times 10^9/L$), neutropenia, lymphocytosis, increased erythrocyte sedimentation rate (ESR) up to 33 mm/h, creatinine and lactate dehydrogenase levels were observed. Anaemia also increased in the course of the disease (haemoglobin decreased from 13.2 to 9.4 g/dL).

The patient was discharged from the hospital on day 10 of admission in a satisfactory condition. A decrease in transaminase and bilirubin levels was observed. Examination of thin blood film revealed asingle *P. vivax*. Primaquine was recommended for two weeks.

DISCUSSION

The peculiarity of this case was the presence of fever and severe abdominal pain at the onset of the disease, which led to the patient's admission to the surgical department and delayed correct diagnosis. At admission to the hospital, the patient did not report a history of malaria, which precluded immediate suspicion of the disease, although in malaria-endemic countries the fever is one of the leading criteria to suspect malaria (9).

Plasmodium vivax malaria is characterised by relapses of malaria because of persistent liver stages of the parasite (10). In countries with a temperate climate, the incubation period, as well as the latency period between illness and relapse may be longer, approximately 8-10 months. This case report also demonstrated the prolonged asymptomatic period before the relapse. Relapses of *P. vivax* malaria can be prevented by aminoquinoline antimalarial. Our pa-

tient had been treated for malaria in India two years before and had not received anti-relapse therapy.

Abdominal pain as a manifestation of malaria is reported in a number of publications (11-13). It is more common in tropical malaria, although it was observed in 27.1% of patients with three-day malaria (*P. vivax*) (3). The localization of pain in the umbilical area is the most frequent. Abdominal pain may be caused by ischaemic bowel changes due to impaired microcirculation as a result of the destruction of red blood cells (12). Other authors also point to circulatory disorders in malaria, which are manifested by generalized spasms of peripheral vessels during chills (13). This can increase the production of biologically active substances such as histamine, serotonin, kinin, prostaglandins, and others. They damage vascular endothelium, increase capillary permeability and blood viscosity, slow down blood flow to the internal organs, and create thromboplastic substances due to haemolysis. Unless there is another cause of pain (cholecystitis, gastritis, etc.), abdominal pain disappears after two days of prescribing specific antimalarial therapy (9), as was in the case presented. It has also been reported that abdominal pain in the cases of *P. falciparum* malaria may be one component of the symptom complex of algid malaria with or without chest pain and arthralgia, and rarely a presenting manifestation of acute pancreatitis (7).

In our case, there was no typical cyclic fever, which is described in patients with malaria (9, 13), although the fever may be irregular at the onset of the disease, which is associated with the asynchronous exiting into the blood of several generations of the pathogen (9). A study from Korea also showed that only 35.7% of patients infected with *P. vivax* had a typical cyclic fever (6). Among other symptoms, the authors point to headache, abdominal pain, nausea and vomiting, which are consistent with our report (6,9). Other researchers have suggested that nausea and vomiting are more common in tropical malaria (9).

One of the symptoms of the malaria-specific triad is splenomegaly. The edge of the spleen was palpated in our case at admission to the hospital (day 8 from the disease onset) and progressed every day, which is typical for three-day malaria (9). In our patient, the liver was also enlarged with impairment of function (hyperbilirubinemia, raised hepatic enzymes). Increased level of hepatic enzymes in patients with three-day malaria was noted by other authors (6), and it characterises moderate or severe disease course (9). Hepatosplenomegaly at the onset of the disease is caused by the increased blood supply to these organs, blood congestion in these organs, lymphoid hyperplasia, as a reaction to red blood cell breakdown and products of vital activity of plasmodia. Hypersplenism may be the main cause of leukopenia and thrombocytopenia (9).

The third specific symptom of malaria is haemolytic anaemia (9, 14). At admission to the hospital, our patient had a normal haemoglobin level (13.2 g/dL), but there was red urine in the absence of significant changes in urine tests and no marked changes in renal function, which could be explained by erythrocyte haemolysis. Jaundice was also observed (although direct bilirubin prevailed at admission). In the course of disease development, a decrease of haemoglobin to 9.4 g/dL and an increase in indirect bilirubin were observed. Other laboratory parameters were characterised by thrombocytopenia, leukopenia, and increased level of lactate dehydrogenase. Other researchers also most frequently observed thrombocytopenia (75%), anaemia, increased level of liver enzymes, lactate dehydrogenase, and coagulopathy (6).

Thus, severe abdominal pain with fever led to a delayed diagnosis of malaria due to the suspicion of acute abdomen and a large number of unnecessary examinations. Delayed diagnosis of malaria can lead to severe complications, such as liver failure, kidney failure, shock, spleen rupture, dehydration, and even death (9, 10). A careful, thorough case history is one of the key points on the way to the correct diagnosis.

Awareness of malaria among physicians and people from malaria-endemic countries should remain high. The rise of the awareness is one of the ways to improve the early diagnosis of rare diseases (15).

CONCLUSION

Severe abdominal pain with fever may be the sign of three-day malaria and cause delayed diagnosis. A careful, thorough case history is one of the key points on the way to the correct diagnosis. There is a need to increase the physicians' awareness of malaria in patients with abdominal pain who have come from malaria-endemic countries.

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Sažetak

Bolovi u trbuhu kod bolesnice s rekurentnom malarijom – prikaz slučaja

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Danas većinu slučajeva malarije u Europi čine međunarodni putnici i imigranti. Tipični klinički znakovi malarije su opetovana groznica, hepatosplenomegalija i hemolitička anemija. Bolovi u trbuhu nisu klinički znak specifičan za malariju. Prikazujemo slučaj trodnevne malarije u 17-godišnjeg mladića iz Indije koji je primljen u Regionalnu dječju bolnicu u Ternopilu s groznicom i jakim bolovima u trbuhu. Ovaj je slučaj zanimljiv zbog prisutnosti groznice i jakih trbušnih bolova pri nastupu bolesti, što je dovelo do prijma bolesnika na kirurški odjel i tako odgodilo postavljanje točne dijagnoze. Pažljivo uzeta iscrpna anamneza jedan je od ključnih koraka na putu do točne dijagnoze. Treba povećati promišljanje liječnika na malariju u bolesnika s bolovima u trbuhu koji dolaze iz zemalja endemičnih za malariju.

Ključne riječi: MALARIJA; BOLOVI U TRBUHU; DIJAGNOSTIKA