CASE REPORT

A 15-year-old boy with travel-imported dengue haemorrhagic fever

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ABSTRACT

Dengue is a viral, mosquito-spread disease with a high prevalence in tropical and subtropical areas. We report a case of travel-imported dengue haemorrhagic fever in a 15-year-old Polish boy. The patient presented with fever, headache, and muscle pain. He was initially diagnosed with influenza. He gradually developed skin rash, mild hepatosplenomegaly, episodic gingival bleeding, and mild symptoms of plasma leakage in the form of palms swelling. The laboratory results revealed leukopaenia and thrombocytopaenia with increasing haematocrit. Dengue virus infection was confirmed by simultaneous detection of NS1, IgM, and IgG antibodies. The patient was treated empirically in the critical phase with satisfactory outcome. The symptoms subsided and the platelet and leukocyte levels gradually reached the normal range for his age.

KEY WORDS:

dengue, travel, haemorrhagic fever.

CASE REPORT

A previously healthy 15-year-old boy presented with high fever, headache, and muscle pain lasting for one day. In addition, he reported one episode of vomiting and loose stool when he was consulted by a family doctor. The symptoms started 5 days after his return from a family holiday in Thailand. It was his fourth visit to this country. The family stayed mostly in the hotel area, although they went on a one-day jungle trip without implementing any malaria prophylaxis. During the journey they were bitten by mosquitos. The patient had been immunized with all routine vaccinations, and an additional one against yellow fever was implemented. Other members of the family showed no symptoms or complaints.

The patient was initially suspected of influenza and received a 5-day course of oseltamivir, prescribed by his doc-tor. He was febrile for the first 2 days of treatment, which was followed by a 24-hour afebrile period. On the fourth day of treatment, he presented generalized maculopapular rash, high fever, fatigue, and muscle pain. He was referred to the regional hospital.

On admission to the regional hospital, he was in a fair general condition, with normal blood pressure, heart rate, and oxygen saturation. On physical examination he had a generalized maculopapular rash without petechiae and mild hepatosplenomegaly; meningeal symptoms were absent. Laboratory test results are presented in Table 1. A chest X-ray was performed and showed no abnormalities. Abdominal ultrasound confirmed mild enlargement of the spleen and liver. The patient was treated empirically with acetaminophen, cyclonamine, antihistaminic drugs, and intravenous fluids.

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TABLE 1. Summary of laboratory data

Parameter	Day 1*	Day 2*	Day 3**	Day 4**	Day 10**
WBC (G/l)	3.3	2.5	3.0	3.7	4.3
RBC (T/l)	5.38	4.77	4.83	5.13	5.36
Hb (g/dl)	15.8	14.1	14.1	14.3	15.4
Hct (%)	48.0	40.9	41.3	42.6	44.6
PLT (G/l)	102	59	61	91	254
INR	1.0	1.0	–	–	–
APTT (s)	30.1	–	–	–	–
Creatinine kinase (U/l)	411	206	–	–	–
D-dimers (ng/ml FEU)	830	820	–	–	–
Albumin (g/l)	–	39	–	–	–
Total protein (g/l)	–	66.8	–	–	–
GGTP (U/l)	20	–	–	–	–
ALT (U/l)	21	23	–	33	70
AST (U/l)	48	39	–	49	45
CRP (mg/dl) (*n*: < 10)	1.7	6.0	–	8.0	–
Total bilirubin (mg/dl)	0.69	0.72	–	–	–

*Regional hospital. **Department of Children Infectious Disease, Warsaw. INR – international normalised ratio, APTT – activated partial thromboplastin time, ALT – alanine transaminase, AST – aspartate transaminase, GGTP – gamma-glutamyltransferase, WBC – white blood cells, RBC – red blood cells, Hb – haemoglobin, Hct – haematocrit, PLT – platelets, CRP – C-reactive protein*

On the second day of hospitalization the patient's general condition deteriorated. The rash became more erythematous, coalescent, and measles-like. The patient was febrile with a maximum temperature of 39.4°C. Laboratory results revealed leukopaenia (2.5 G/l) and thrombocytopaenia (59 G/l). On the following day he was transferred to the Department of Children's Infectious Disease, Medical University of Warsaw for further diagnostics and treatment. His condition was stable.

On admission to our department the patient presented with a lacy, net-like looking rash on the chest and arms, swollen, reddish flush hands, and mild submandibular lymphadenopathy. He was afebrile with enanthema located on mucosal membranes of the hard palate, and palatopharyngeal arches, liver, and spleen were palpable 1.5 cm below the costal margin. The white blood cell count increased to 3.0 G/l, the platelets count increased insignificantly 61 G/l, and haematocrit was 41.3%. The peripheral blood smear for malaria parasites and the immunochromatographic fast blood test (OptiMAL-IT) were negative. The presence of dengue NS1 antigen as well as dengue virus-specific IgM and IgG antibodies were positive by the fast immunochromatographic test (SD BIOLINE Dengue Duo). The genome analysis of the virus was not available.

Infection with dengue virus was confirmed. The patient continued symptomatic treatment with cetirizine, cyclonamine, and intravenous fluids. During the hospitalization his life parameters stayed closer to the low border of the norms for his age. The lowest noted blood pressure was 104/55 mmHg during the day and 92/72 mmHg at night. One episode of gingival bleeding during con-

sumption of an apple was observed, which resolved spontaneously. On the sixth day of hospitalization linear petechiae on the arms appeared. The platelet count was gradually increasing without the need for transfusion. The patient stayed afebrile, and the rash gradually subsided as well as the palm oedema, liver and spleen were unpalpable. He was released from the hospital after 10 days of observation and empirical treatment. The laboratory findings showed an increase in platelet count of 254 G/l, leukocytes count of 4.3 G/l, and slightly elevated alanine aminotransferase of 70 U/l. On release we recommended a control central blood count and alanine aminotransferase in 2 weeks, proper fluid intake, home rest, and limited physical activity until the follow-up visit to a GP.

DISCUSSION

Dengue has become one of the most widespread mosquito-borne disease globally. Up to 400 million people are infected with dengue annually, with approximately 100 million infection cases, and 22,000 deaths from severe dengue [1]. The spectrum of the disease ranges from asymptomatic to severe haemorrhagic manifestations and critical plasma leakage. The primary infection to 1 of 4 viral serotypes may not present any clinical manifestations and provides life-long immunity only to this serotype [2]. However, the secondary and subsequent infections tend to manifest as a dengue haemorrhagic fever (DHF) or even dengue shock syndrome (DSS). Mild symptoms of dengue like fever, headache, and muscle pain can easily be confused with other common illnesses.

The patient was initially suspected of influenza infection, and the history of recent travel to a country where dengue is an endemic infection was crucial to broadening the spectrum of differential diagnosis. He was at high risk of developing a more severe form of dengue infection due to multiple travels to dengue endemic areas in the past. Moreover, the family visited the jungle without implementing any prophylaxis against mosquito bites. Epidemiologic, clinical, and virological studies of DHF/DSS in humans have shown a significant association between the dengue vascular permeability syndrome and dengue virus infection in the presence of circulating dengue antibodies, whether transmitted passively from mother to child or actively acquired from previous infection. The risk for developing vascular permeability syndrome is inversely correlated with age; the youngest children are at highest intrinsic risk [3].

Our patient presented a biphasic fever characteristic for dengue. He was admitted to the clinic in the critical (afebrile) phase of the disease. The crucial point of care was awareness of warning signs of impending vascular permeability like persistent vomiting, severe abdominal pain, rising haematocrit, and decreasing platelet value [3]. He gradually developed skin rash, mild hepatosplenomegaly, episodic gingival bleeding, and mild symptoms of plasma leakage in the form of palms swelling. The laboratory results revealed leukopaenia and thrombocytopaenia with increasing haematocrit. During the 24-36-hour period of crisis the patient had to be closely monitored. He met the clinical criterial of dengue haemorrhagic fever and displayed warning signs for severe dengue (Table 2). The clinical manifestations strongly suggested consecutive infection with one of the dengue virus subtypes.

The treatment of dengue is supportive. At the early stage of infection intravenous resuscitation with isotonic crystalloid in accordance with vital signs, blood pressure, and urine output was used. However, in the critical phase we had to reduce the crystalloid input to prevent fluid overload. Initially, he received acetaminophen to control fever and relieve pain [4]. In cases of dengue fever aspirin and all nonsteroidal anti-inflammatory drugs (like ibuprofen) should be avoided because of their anticoagulant properties [5]. The critical period began with defervescence. Frequent monitoring of vital signs and careful observation for early shock symptoms was crucial [6].

Dengue infection was confirmed by detection of NS1 protein, which circulates in blood during the acute illness. Non-structural protein 1 (NS1) of the dengue viruses is a viral toxin that contributes to dengue pathogenesis by mechanisms analogous to those of bacterial endotoxins in toxic shock syndrome [7]. The presence of IgG antibodies confirmed the consecutive infection with a new serotype of dengue virus. The IgG antibody concentrations are abundant in secondary but minimal in primary dengue virus infection [3].

We would like to draw attention to the popularity and affordability of exotic travel destinations, resulting in wide spread of tropical diseases outside of their endemic prevalence. Due to the fact that initial symptoms of dengue virus infection are nonspecific, patients' history taking in regard to recent trips and destinations is crucial. As in the presented case, the popularity of frequent trips to endemic regions presents us with the challenge of more severe clinical manifestations of the disease. Travelers to exotic destinations should review country-specific travel recommendations, health notices, and warnings at least 4-6 weeks before travel. In addition, they should attend a travel clinic and receive information about available prophylactical measures like vaccinations. Moreover, tourists should familiarize themselves with the principles

TABLE 2. World Health Organization 2015 Dengue Case Definitions [9]

Dengue	Severe dengue

Dengue is defined by fever as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms:
• nausea/vomiting;
• rash;
• aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia);
• tourniquet test positive;
• leukopenia (a total white blood cell count of < 5,000/mm³), or any warning sign for severe dengue:
  – abdominal pain or tenderness,
  – persistent vomiting,
  – extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites),
  – mucosal bleeding at any site,
  – liver enlargement > 2 centimetres,
  – increasing hematocrit concurrent with rapid decrease in platelet count.
	Severe dengue is defined as dengue with any one or more of the following scenarios:
	• severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress; a high hematocrit value for patient age and sex offers further evidence of plasma leakage;
	• severe bleeding from the gastrointestinal tract (e.g., hematemesis, melena) or vagina (menorrhagia) as defined by requirement for medical intervention including intravenous fluid resuscitation or blood transfusion;
	• severe organ involvement, including any of the following:
	  – elevated liver transaminases: aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 1,000 (U/l),
	  – impaired level of consciousness and/or diagnosis of encephalitis, encephalopathy, or meningitis,
	  – heart or other organ involvement including myocarditis, cholecystitis, and pancreatitis.

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of preventing mosquito bites, such as using insect repellents, wearing long-sleeved shirts and long trousers, using 0.5% permethrin to treat clothing and gear, and staying in screened rooms or using mosquito nets at night [8]. These measures are crucial in the prevention of the spread of dengue, but also other mosquito-borne infections like zika or chikungunya virus.

DISCLOSURE

The authors declare no conflict of interest.

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