

Case Report

Case report of severe dengue fever complicated by megaloblastic anemia and type 1 diabetes mellitus

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Abstract: This study aimed to explore the clinical characteristics, diagnosis, treatment, and preventive measures for a severe dengue fever patient with megaloblastic anemia and type 1 diabetes. The study used a dengue infection case diagnosed in the local hospital on August 13, 2024, and analyzed its clinical symptoms, epidemiologic data, laboratory test results, and treatment. The patient had a history of residence in Guangzhou and presented with symptoms such as nausea, vomiting, diarrhea and fever without any clear trigger. The results of dengue NS1 antigen detection and nucleic acid testing were both positive. Laboratory tests revealed that the patient's leukocyte count, platelet and hemoglobin levels were progressively decreasing. After receiving symptomatic treatments such as oxygen inhalation and monitoring, cardiac monitoring, nutritional support, blood glucose monitoring, gastric protection, and maintenance of water and electrolyte balance, the patient's condition improved and the patient was discharged. The clinical manifestations of dengue fever are complex and diverse. Currently, there are no specific antiviral drugs available. The treatment is based mainly on symptomatic management. The prognosis of patients is usually favorable.

Keywords: Dengue fever, megaloblastic anemia, type 1 diabetes mellitus, severe dengue, case report

Introduction

Dengue fever (DF) is an acute mosquito-borne infectious disease caused by the dengue virus [1]. With the increasing convenience of transportation and the growing frequency of population mobility in China, imported and local cases of dengue fever have been reported in several provinces [2].

The diagnosis of dengue fever is based on the epidemiologic history, clinical manifestations, and laboratory findings, including NS1 antigen detection or viral nucleic acid testing during the acute phase [3]. Currently, there are no specific antiviral drugs. The treatment mainly involves symptomatic and supportive therapy, with the focus being on maintaining fluid balance, using acetaminophen to reduce fever, and close monitoring for warning signs [4]. Severe cases require hospitalization and intensive support-

ive treatment [4]. Most patients have a good prognosis and usually recover within 2 weeks.

This study conducted a comprehensive analysis and summary of a case of severe dengue fever that was admitted to our hospital and was accompanied by megaloblastic anemia and type 1 diabetes. The aim was to provide a reference for the clinical diagnosis and prevention and control of dengue fever.

Case report

The patient was a 17-year-old female. The patient recently traveled to Haikou and had a travel history in Guangzhou on July 13. Both of her parents tested positive for dengue virus nucleic acid recently. She reported experiencing nausea and vomiting without any obvious cause on August 12, along with 5-6 episodes of diarrhea per day and a body temperature of 38.5°C.

Table 1. Routine blood test results

Indicator	August 12	August 13	August 15	August 17	August 22	August 30	Reference Range
Leukocyte Count ($\times 10^9/L$)	2.72	2.25	2.36	2.84	20.25	5.86	4.0-12.0
Platelet Count ($\times 10^9/L$)	46	39	70	68	563	674	150-450
Neutrophil (%)	24.5	21.7	33.9	23.1	65.1	51.7	37-77
Lymphocyte (%)	70.4	72.9	59.9	57.2	29.2	40.5	17-54
Monocyte (%)	3.2	2.7	3.4	5.2	4.3	6.7	2-11
Hemoglobin Concentration (g/L)	47	46	75	78	92	102	114-154
Mean Corpuscular Volume (fL)	101.8	102.5	103.6	102.7	101.2	96.5	80-100
Red Blood Cell Count ($\times 10^{12}/L$)	1.72	1.68	2.83	2.85	3.86	4.05	4.0-5.5

Despite taking oral medications, she got no significant relief. To seek further treatment, she visited the emergency department of The First Affiliated Hospital of Hainan Medical University. Laboratory tests are shown in **Table 1**. The patient reported a 3-year history of type 1 diabetes. Previously, she had been treated with an insulin pump and her blood glucose was maintained below 10 mmol/L. She was admitted to the emergency observation ward for fever and diarrhea.

The patient was given nutritional support, and antipyretic and antidiarrheal treatments immediately after admission. As the cause of the patient's fever was unknown upon admission and both parents had tested positive for dengue fever, it was suspected that the patient might have been infected. Therefore, blood samples were immediately collected and sent to the laboratory for dengue NS1 antigen testing. On August 14th, the test results were positive for dengue NS1 antigen. The infection was reported to the Infection Control Department, and blood samples were collected from the patient by the municipal Center for Disease Control and Prevention (CDC) for dengue nucleic acid testing. On August 16th, the municipal CDC informed that the patient had tested positive for dengue virus type 1 (DENV-1) nucleic acid, and she was diagnosed with dengue fever. The patient was immediately placed in a single room for isolation, and mosquito nets were used to prevent mosquito bites and interrupt transmission. On August 13th, a re-examination of the blood routine showed a platelet count of $39 \times 10^9/L$ and a continuous decline, indicating a high risk of bleeding. The patient was notified of her critical condition. Symptomatic treatment was given, including oxygen supply monitoring, electrocardiogram monitor-

ing, nutritional support, blood glucose monitoring, gastric protection, and maintenance of fluid and electrolyte balance. Blood platelets and suspended red blood cells were transfused to the patient. Subsequent blood routine re-examinations were performed to monitor platelet levels dynamically, and the patient's skin and mucous membranes were closely observed for signs of bleeding. On the afternoon of August 13th, the patient received insulin pump treatment for blood glucose control and dynamic monitoring. On August 15th, the patient's body temperature was 36.8°C. The patient continued to receive platelet and packed red blood cell transfusions.

On August 16th, the patient's bone marrow morphology examination showed that erythroid cells were significantly proliferating, composed mainly of mid and late erythrocytes. At the late erythrocyte stage, an imbalance between the nucleus and cytoplasm during development was observed, and morphologic changes similar to megaloblastic erythrocytes were also noted. The nutritional anemia tests results indicated that the patient had low serum folate and vitamin B₁₂ levels (as shown in **Table 2**). That afternoon, the patient received injections of vitamin B₁₂ and mecobalamin, combined with a subcutaneous injection of granulocyte colony-stimulating factor. On August 18th, a spiral computed tomography (CT) scan showed pelvic and abdominal effusions, multiple mildly enlarged retroperitoneal and mesenteric lymph nodes, pericholecystic effusion, mild to moderate bilateral pleural effusion, and bilateral pulmonary atelectasis. On August 22nd, the patient's appetite and sleep condition were good, without fever or diarrhea symptoms. Both white blood cell and platelet counts had returned to normal ranges, and the patient remained under

Table 2. Nutritional anemia: serologic tests results

Indicator	Results	Reference Range
Serum Iron	3.1	9.0-30.4 (μmol/L)
Total Iron-Binding Capacity	50.0	44.8-71.6 (μmol/L)
Transferrin	2.00	2.50-3.80 (g/L)
Transferrin Saturation	6.20	20-55 (%)
Serum Vitamin B12	108.96	133.0-675.0 (pmol/L)
Serum Ferritin	25.3	11.0-306.8 (ng/mL)
Serum Folate	7.45	9.00-45.10 (nmol/L)

clinical observation. After 10 days of hospitalization, the patient's body temperature returned to normal and gastrointestinal symptoms significantly improved, indicating a good therapeutic response. The patient was discharged on August 23, 2024, after complete resolution of clinical symptoms. One week after discharge, the patient visited the hematology outpatient department for follow-up examination on August 30, 2024. The laboratory tests showed that the patient's blood routine, liver function, kidney function, and serum electrolyte indicators were all within the normal reference range.

Discussion

The main pathogenic mechanism of dengue infection is the formation of antigen-antibody immune complexes between the virus and the antibodies derived from the host [5]. These complexes can further activate the complement system and increase vascular permeability, resulting in clinical manifestations such as vasoconstriction, bleeding, and even shock [5]. Additionally, the virus inhibits bone marrow hematopoietic function and reduces the production of leukocytes and platelets. The early clinical warning signs of severe dengue include severe abdominal pain, frequent vomiting, bleeding tendency, and prolonged high fever for more than one week [6]. Laboratory warning indicators include rapid decline in platelet count, hypoproteinemia, and significant elevation in cardiac enzymes, bilirubin, D-dimer, and brain natriuretic peptide levels. Imaging warning signs include serous cavity effusions and arrhythmia [6].

Megaloblastic anemia is caused mainly by folate or vitamin B₁₂ deficiency. Its core pathologic feature is the inhibition of hematopoietic function, manifested as insufficient reserve of the entire hematopoietic system, accompanied

by impaired cellular and humoral immune functions as well as dysregulated inflammatory responses [7]. Dengue fever often causes gastrointestinal symptoms, including vomiting, diarrhea and abdominal pain [8]. These symptoms significantly impair intestinal absorption of folate and vitamin B₁₂, thereby exacerbating the severity of MA.

Hyperglycemia intensifies systemic oxidative stress and amplifies the systemic inflammatory cascade triggered by dengue virus infection. Therefore, compared to non-diabetic DF patients, the clinical manifestations in T1DM patients (including myalgia, fatigue, headache, and fever) are significantly more severe [7]. At the same time, hyperglycemia damages the gastrointestinal mucosal barrier, interacts synergistically with intrinsic gastrointestinal symptoms related to DF (vomiting, abdominal pain, and diarrhea), and further increases the risk of electrolyte disorders [9]. In parallel, the antigen-antibody immune complexes derived from DENV can activate the complement cascade reaction and release large amounts of pro-inflammatory cytokines, causing secondary damage to the endothelial cells and leading to a synergistic increase in vascular permeability [10]. Under the combined effect of these two pathologic insults, patients develop typical warning signs of severe dengue at an earlier stage and are more susceptible to these manifestations.

The diagnosis of dengue fever in this patient was well-established. The NS1 antigen and nucleic acid test results were both positive, and combined with the clinical manifestations, confirmed the diagnosis of dengue fever. In addition, the patient had an elevated MCV, decreased vitamin B₁₂ and folic acid levels, and megaloblastic changes in the bone marrow morphology. A diagnosis of megaloblastic anemia was established, and the patient also had a history of type 1 diabetes. Notably, this case had not merely the coexistence of dengue fever and hematologic abnormalities, but rather the coexistence of three diseases, that mutually aggravated each other. Upon admission, the patient already presented with gastrointestinal symptoms, platelet count below 50×10⁹/L, and multiple pleural effusions. These findings constituted early warning signs of severe dengue,

indicating that the patient was at high risk of developing severe disease.

Based on this case, we propose the following clinical recommendations. In the diagnosis and management of dengue fever, vitamin B₁₂ and folate levels should be actively screened in patients with concomitant anemia to avoid misdiagnosing megaloblastic anemia as dengue-related bone marrow suppression or hemorrhagic anemia. For patients with clear signs of severe illness, precise fluid management should be implemented to avoid either insufficient or excessive fluid administration. For patients with concomitant type 1 diabetes, close monitoring of blood glucose levels and adjustment of insulin dosage are required, along with early supplementation of folic acid and vitamin B₁₂ to promote hematopoietic recovery. In summary, this case highlighted that early multidisciplinary intervention may improve prognosis when severe dengue fever coexists with other underlying conditions.

Conclusion

Dengue fever can present with complex and overlapping manifestations, especially when complicated by other hematologic and metabolic disorders. This case underscores the importance of thorough laboratory evaluation and multidisciplinary supportive management.

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Written informed consent was obtained from the patient's legal guardian for publication of this case report.

Disclosure of conflict of interest

None.

Abbreviations

CDC, Center for Disease Control and Prevention; DENV-1, Dengue Virus Serotype 1; MCV, Mean

Corpuscular Volume; CT, Computed Tomography; DF, Dengue Fever; MA, Megaloblastic Anemia; T1DM, Type 1 Diabetes Mellitus.

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