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Dengue Virus: Imported Case Report and Risk of Emergence in Morocco

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Abstract

Dengue, caused by the dengue virus, is one of the most widespread arboviral diseases globally, with approximately 100 to 400 million infections annually. Transmitted by Aedes aegypti and Aedes albopictus mosquitoes, the disease affects over 100 countries, primarily in tropical and subtropical regions. Although most infections are asymptomatic or mild, dengue can progress to severe forms, such as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), leading to high mortality rates in the absence of appropriate treatment.

We present here a case of DENV infection in a Moroccan woman returning from Senegal and we discuss the importance of considering arboviral infections after traveling to an endemic area, diagnosis tools and the risk of the emergence of DENV in Morocco due to climate change and increased population mobility.

Keywords: Dengue virus, Diagnosis, Emergence, Imported case, Morocco

Introduction

Dengue virus (DENV) is the most widespread mosquito-borne viral infection in humans. It has a global distribution, with an estimated 400 million infections annually, and its geographical spread continues to expand. More than 100 countries worldwide experience dengue outbreaks [2,4,5]. According to the World Health Organization (WHO), the global incidence of dengue is rising. Over 7.6 million cases had been reported in 2024, including 3.4 million confirmed cases and more than 3,000 deaths. A significant surge has been observed in the Americas and Southeast Asia, as well as in several European countries [6] (Figure 1). This increase is attributed to factors such as climate change, rapid urbanization and increased human mobility, all of which contribute to the spread of the mosquito vectors responsible for dengue transmission [6]. In response, WHO launched a global strategic plan in October 2024 to combat dengue and other vector-borne diseases, aiming to enhance surveillance, prevention, and outbreak response [6]. We present here a case of DENV infection in a Moroccan woman returning from Senegal and we discuss the importance of considering arboviral infections after traveling to an endemic area, diagnosis tools and the risk of the emergence of DENV in Morocco due to climate change and increased population mobility.

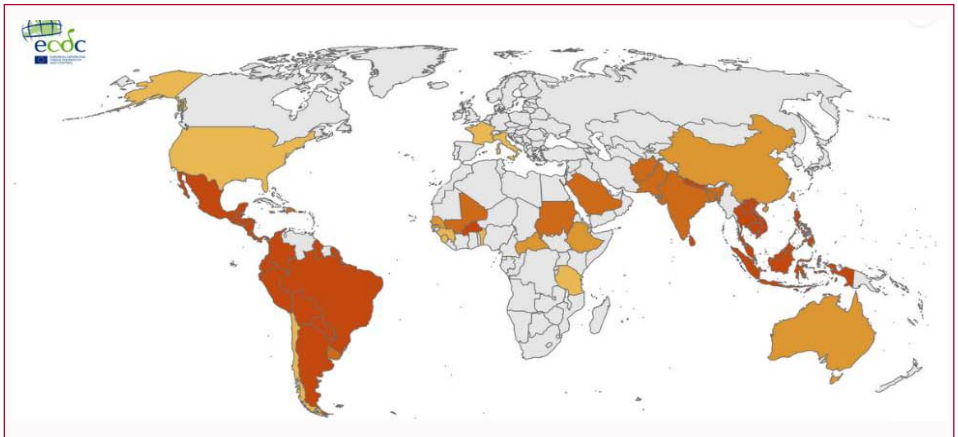

Figure 1: Notification rate of dengue cases over three months per 100,000 inhabitants, October-December 2024 (7).

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Case Presentation

A Moroccan 39-year-old female was admitted on 11/15/2024 for febrile syndrome following her return from an endemic country (Senegal), on 11/10/2024. She had spent two weeks in Senegal without antimalarial chemoprophylaxis. Her surgical history included two cesarean deliveries. No notable allergic or family history was reported. Symptoms began four days before admission, including fever (39°C), generalized abdominal pain, headache, nausea, vomiting, dizziness, epistaxis, and generalized fatigue. On admission, the patient was conscious, hemodynamically and respiratory stable and febrile (39°C). The patient had intense headaches and was vomiting multiple times a day. Abdominal examination revealed a cesarean scar with a soft abdomen, without palpable mass or hepatosplenomegaly.

Skin and mucosal examination showed no jaundice or purpuric lesions but the presence of petechiae. No rash was observed. Other system examinations were unremarkable. An abdominal Computed Tomography scan was unremarkable. Blood and urine samples were collected, below is a summary of the results of the biological tests requested during the hospitalization, showing the evolution of each parameter (Table 1).

Table 1: Biological tests requested during the hospitalization.

Parameters	15-11-2024	16-11-2024	17-11-2024	19-11-2024
Hematology				
Hemoglobin (g/dl)	12	12	12,7	12,4
Hematocrit (%)	35,6	35,8	37,8	36,4
White Blood Cells (/ul)	2000	3300	4400	5100
Neutrophils (/ul)	900	1400	800	1800
Lymphocytes (/ul)	800	1600	2800	2300
Platelets (/ul)	93000	69000	71000	163000
D-Dimers (ug/ml)	1,7	1,8	-	1,2
Biochemistry				
ASAT (UI/l)	96	257	206	195
ALAT (UI/l)	105	220	211	219
GGT (U/L)	38	-	48	81
LDH (UI/l)	380	-	494	429
CRP (mg/l)	4,2	5	6,8	2,3
Ferritin (ng/ml)	370	-	416	-

The patient presented with leukopenia (2,000/µl), lymphopenia (900/µl), and neutropenia (800/µl), along with thrombocytopenia (69,000/µl) and a reduced hematocrit level (35.6%). Hepatic involvement was noted, with cholestasis and hepatic cytolysis. Testing for *Plasmodium* spp. were negative. Viral serologies for HIV, HAV, HBV and HCV were also negative. Serologic testing for Epstein-Barr virus (EBV) revealed positive IgG anti-EBNA and IgG anti-VCA, with negative IgM anti-VCA, indicating past infection. Similarly, cytomegalovirus (CMV) serology showed positive IgG and negative IgM, suggesting a prior exposure. Arbovirus screening was negative for Chikungunya and Zika viruses. However, dengue serology showed positive IgM and IgG, indicative of an active infection. Blood and urine PCR confirmed the presence of DENV RNA.

Under symptomatic treatment, the patient's condition improved progressively, with normalization of platelet count, white blood cells and hematocrit levels. She had a favorable clinical evolution and was discharged on 11/19/2024.

Discussion

The DENV is a single-stranded, positive-sense RNA virus belonging to the *Flavivirus* genus within the *Flaviviridae* family. Other notable arboviruses in this family include the Japanese encephalitis virus (JEV), the West Nile virus (WNV) and the yellow fever virus (YFV) [1]. Four distinct DENV serotypes [1-4] have been identified worldwide, each with unique antigenic properties. Additionally, a fifth serotype (DENV-5) was first detected in the blood of a patient in Sarawak, Malaysia, in 2007 [3].

Dengue is transmitted to humans through the bite of infected female mosquitoes of the *Aedes* genus, particularly *Aedes aegypti* and *Aedes albopictus* [2]. Recently, countries such as Senegal, Burkina Faso, Nigeria, and Ethiopia have reported significant case numbers, according to Africa CDC data [13]. The WHO reports a ninefold increase in dengue infections across Africa in 2023 compared to 2019 [14]. This epidemiological trend underscores the critical need for Moroccan clinicians to systematically consider arboviral diseases in their differential diagnoses, as these infections continue to expand across Africa and globally.

Previous studies have suggested that viral factors contribute to the pathogenesis of this disease, including the viral NS1 antigen and its antibodies, viral variations and virulence, sub-genomic RNA and the presence of cross-reactive memory T cells [4]. In humans, a dengue serotype provides lifelong immunity against reinfection with the same serotype but only temporary and partial immunity against other serotypes. Due to the phenomenon of antibody-dependent enhancement, reinfection with a different serotype can increase the risk of developing a severe, potentially fatal form [1,2]. The clinical manifestations of dengue infection vary significantly, ranging from asymptomatic infection to severe hemorrhagic forms with multiorgan failure and death in up to 13% of untreated cases [2]. Three clinical forms of dengue are distinguished: the mild form, known as dengue fever (DF); the severe form, or dengue hemorrhagic fever (DHF), characterized by hematomas and severe thrombocytopenia; and the most critical stage, dengue shock syndrome (DSS). DSS involves coagulation abnormalities, increased vascular fragility, high plasma leakage, and capillary permeability leading to hypovolemic shock and an increased risk of multiorgan failure [5]. Our patient, a 39-year-old woman returning from an endemic region, exhibited classic symptoms of dengue, including high fever, headache, abdominal pain, nausea, and vomiting.

Laboratory findings revealed leukopenia, lymphopenia, thrombocytopenia, and hepatic cytolysis, consistent with early critical phase, with risk of progression to severe dengue. Dengue most often resolves within a week. However, in 2 to 4% of cases, severe forms can occur suddenly after 3 to 5 days of illness progression. When this aggravation occurs, the outcome can rapidly become fatal. Risk factors for severe dengue include pregnancy (particularly in the third trimester), extreme ages of life, and chronic conditions such as diabetes, obesity, heart failure, asthma, chronic liver diseases and major sickle cell syndromes [5].

Diagnosis of DENV infection in our patient was confirmed by blood positive IgM and IgG antibodies (Dengue Virclia® IgG / IgM Monotest, Vircell) and blood detection of viral RNA by RT-PCR (RealStar® Dengue RT-PCR Kit 3.0, Altona Diagnostics). Accurate diagnosis of dengue is essential for effective clinical management

and surveillance. However, the clinical presentation of dengue is nonspecific and overlaps with other febrile illnesses, making biological confirmation crucial. The CDC (Centers for Disease Control and Prevention - United States) recommends two primary strategies for early diagnosis (within the first 7 days after symptom onset) [2]:

- Rapid immunochromatographic antigen tests targeting the non-structural glycoprotein 1 (NS1), combined with IgM detection by Enzyme-Linked Immunosorbent Assay (ELISA).
- Nucleic acid amplification tests (real-time RT-PCR) combined with IgM serology.

However, each of these methods has significant limitations. For example, although IgM ELISA is often considered the preferred diagnostic method, IgM antibodies are only detectable from 4 to 5 days after the onset of symptoms and for about 12 weeks.

This means that IgM ELISA tests could provide false-negative results during the critical early days of the illness. Conversely, IgM antibodies sometimes lack specificity, which can lead to false positives due to non-specific reactivity (Malaria, Typhoid fever, Cytomegalovirus…) [2]. Seroneutralization tests, which require the use of infectious viruses and are systematically performed at the CNR, have better specificity compared to traditional ELISA or CLIA tests.

On the other hand, The NS1 antigen is detectable from 1 to 2 days after the onset of symptoms, with a peak typically between the 3rd and 7th day. The NS1 antigen test offers several advantages, such as low cost, ease of use and rapid results, making it effective in endemic areas with high incidence and limited resources. However, the sensitivity of available NS1 antigen tests varies significantly depending on the DENV serotype, with an overall sensitivity of 71% (95% CI: 61–79%). This sensitivity fluctuates by serotype: ranging from 50% to 90.9% for DENV-1, 38.5% to 85.7% for DENV-2, 46.7% to 91.3% for DENV-3, and 21.7% to 87% for DENV-4 [15]. Additionally, sensitivity may be further reduced during secondary infections**.** In this regard, combining direct and indirect methods improves diagnostic accuracy [2]. Commercial ELISA (Enzyme-Linked ImmunoAssay) kits for DENV NS1 antigen detection, such as Platelia® Dengue NS1 (Bio-Rad) and Pan E-Dengue Early ELISA®, Panbio, offer automated, rapid, and user-friendly testing solutions. These assays demonstrate high analytical performance with specificity ranging from 97.9% to 100% and sensitivity between 58.1% and 93.3% according to HAS dengue guidelines. Additionally, combined rapid diagnostic tests (RDTs) capable of simultaneous detection of NS1 antigen and anti-Dengue IgG/IgM antibodies - including the One Step Dengue NS1Ag + IgG/IgM Test® (SD Bioline) and Panbio Early Rapid NS1 + Panbio Dengue Duo Cassette® (Panbio), are now available, with reported sensitivity exceeding 88%.

RT-PCR for detecting DENV RNA is considered the most sensitive and specific method. However, its performance depends on viral kinetics, viral RNA becomes undetectable beyond 5 days after symptom onset, potentially leading to false-negative results if testing occurs too late. The WHO recommends specimen collection within this 5-day window for optimal RT-PCR detection of DENV [16]. RT-PCR offers many advantages, such as the ability to serotype DENV and perform differential diagnosis of various arbovirus infections. Furthermore, RT-PCR technology is rapidly evolving and an increasing number of manufacturers are offering closed, ready-to-use systems that are simple to operate and capable of providing results in just one hour. Some ready-to-use kits that provide results quickly are the Altona RealStar® Dengue RT-PCR Kit 2.0 and the ZIKV/DENV/CHIKV REALTIME PCR KIT [2].

The risk of the emergence of indigenous dengue cases and its spread in Morocco is influenced by several factors. Although *Aedes aegypti*, the primary vector of the dengue virus (DENV), has not been reported in Morocco, *Aedes albopictus* has been detected in certain regions, particularly in urban and semi-urban areas. In September 2015, *Aedes albopictus* was identified for the first time in the Rabat region. Subsequent studies confirmed its ability to transmit several arboviruses, including DENV, chikungunya (CHIKV), Zika (ZIKV), and yellow fever (YFV) [17]. Predictive models suggest that northwestern and central parts of Morocco, especially urban areas, provide favorable habitats for *Aedes albopictus*, increasing the risk of local transmission of these viruses [17,18]. Its geographical expansion may be facilitated by favorable climatic conditions such as high temperatures and rainfall, which support mosquito breeding. In Morocco, especially during the summer months, the increasingly warm climate promotes the proliferation of mosquito vectors.

Recent climatic data shows a significant warming trend in Morocco, with temperatures rising by about 1.1°C between 1981 and 2016. 2020 and 2022 being the hottest years on record, exceeding the 1981–2010 average by 1.4°C and 1.63°C, respectively.

Rainy periods further encourage mosquito settlement in urban environments, where conditions like stagnant water create ideal breeding grounds for their development.

In parallel, in recent years, the number of Moroccan tourists traveling to countries where dengue is endemic has increased exponentially [12]. Economic and diplomatic relations between Morocco and various countries in Africa and Asia have also strengthened significantly. Consequently, the risk of importing pathogens into Morocco from abroad and local transmission has considerably increased. Moreover, the organization of international events like the Africa Cup of Nations in 2025 and the World Cup in 2030 brings thousands of visitors from

countries where dengue is endemic (such as Southeast Asia, Latin America, etc.). This increases the risks of imported cases and the introduction of the virus into the local population. Additionally, the rise in international travel, particularly for large-scale events, can lead to the importation of dengue cases. These cases could become potential vectors for the epidemic if local mosquitoes are present and capable of transmitting the virus.

Although Morocco has not yet reported any indigenous cases of dengue, the presence of *Aedes Aegypti* and the increase in international travel put the country at an increased risk of the disease's emergence. Morocco's epidemiological surveillance, although strengthened in recent years, needs to be adapted to detect any suspected dengue cases early.

Rapid screening, confirmation of cases, and prompt response are essential to prevent the spread of the virus. Public and healthcare professional awareness is also an important factor. Furthermore, monitoring mosquito habitats and control measures (such as eliminating stagnant water and spraying insecticides) is crucial. Protective measures (such as using mosquito nets, repellents, etc.) should be encouraged, especially in high-risk areas.

Finally, there is no antiviral therapy available for DENV infection. However, two dengue vaccines have been approved and are available

in several countries. Dengvaxia, a vaccine developed by Sanofi Pasteur, has been authorized in several dengue-endemic countries and Qdenga approved and licensed in certain countries in 2022 [4]. However, Qdenga is only recommended for the age group of 6 to 16 years in high-transmission settings [8]. Several additional vaccines are currently under evaluation.

Conclusion

Dengue represents a growing global burden, with approximately 100 to 400 million infections reported each year. Factors such as climate change, urbanization, and population mobility contribute to the geographic expansion of the disease and increase the risk of epidemics. The case of DENV infection presented here highlights the clinical and diagnostic challenges associated with this globally significant arboviral disease. Prevention and early detection are key pillars in limiting mortality associated with severe dengue.

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