Increase in dengue fever imported from Côte d’Ivoire and West Africa to France

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Abstract

Dengue is usually not considered a significant health problem in Africa because severe forms of dengue illness are rarely reported. In the absence of local surveillance data, the investigation of dengue cases imported to France contributed to document the circulation of dengue virus in this area. From 1 July 2006 to 31 December 2008, a total of 148 dengue cases imported to metropolitan France were reported through the mandatory notification system. Arthralgia and signs of severity (haemorrhage, thrombocytopenia) were less frequent in patients returning from West African countries. DENV-3 was isolated in two patients from Côte d’Ivoire in 2008. The number and proportion of patients returning from Côte d’Ivoire to France increased significantly in 2008 compared with the previous 18-month period. In parallel, the marginal increase in air travel does not explain the high increase observed in imported dengue cases to France. Our data illustrate increased dengue circulation and the emergence of DENV-3 in this area, with public health implications for epidemiological surveillance and case management locally.

Keywords: Dengue; West Africa; Côte d’Ivoire; France; mandatory reporting; DENV-3.

Introduction

The genus Flavivirus includes pathogens with a huge impact on human health through diseases such as yellow fever, West Nile fever and dengue fever. Dengue can be caused by one of the four distinct serotypes of dengue virus (DENV). The transmission of dengue serotype 2 (DENV-2) in an enzootic cycle involving monkeys and several species of
mosquitoes has been documented in West African forests.\cite{1,2} In West African countries (WAC), dengue can also occasionally be transmitted in an urban cycle involving humans and anthropophilic mosquitoes belonging to *Aedes* spp.\cite{1,3} Little information, however, is available on the magnitude of transmission in urban environments in WAC. In the past 20 years, serosurveys evidenced circulation of mainly DENV-2 in WAC, especially in Senegal.\cite{4,5} DENV-4 has also been isolated in Dakar residents.\cite{4} Ten years ago, DENV-1 was isolated from a French soldier living in Abidjan, Côte d’Ivoire.\cite{6} In the context of a yellow fever epidemic lasting from April to July 2008 in Abidjan, DENV-3 was typed by polymerase chain reaction (PCR) in one patient returning from Abidjan to France\cite{7,8} and one returning to Japan.\cite{9} To our knowledge, DENV-3 has not been previously isolated in patients from West African countries.

Dengue is usually not considered a significant health problem in Africa because severe forms of dengue illness are rarely reported.\cite{10} In a context of high malaria incidence and in the absence of dengue-specific preventive or curative treatments, most West African countries have not implemented specific dengue surveillance systems and often lack laboratory capacity to diagnose dengue infection. The circulation of dengue viruses in the area is likely, therefore, to be underestimated. Furthermore, the introduction of a new serotype, previously observed in the Americas, Asia, the South Pacific and East Africa,\cite{11}, but never in West African countries, could have an important epidemic potential and be associated with a higher proportion of secondary infections and severe forms.\cite{12,13} In the absence of local surveillance data, the investigation of imported dengue cases to France contributes towards documenting dengue virus circulation in this area.

**Material and methods**

Notification by French physicians of clinically confirmed dengue infections became mandatory in July 2006 for surveillance purposes and to guide intervention in some French départements where *Aedes albopictus*, a potential vector of dengue virus, is established. Notifications seek to document viraemic cases and apply only to recent infections, i.e. cases where the onset of symptoms is less than seven days old. Cases are confirmed either by PCR or by serology (detection of dengue-specific IgM). This information is centralized by the Institut de Veille Sanitaire, the French institute for public health surveillance. We compared the characteristics of the patients returning to metropolitan France (continental France and Corsica) from West African countries or from other countries.

**Results**

From 1 July 2006 to 31 December 2008, a total of 148 dengue cases imported to metropolitan France (mainland France plus Corsica) were reported through the mandatory notification system. Of these patients, 69 (47%) came from the French Overseas Territories (58 from French West Indies, eight from French Polynesia, two from French Guiana and one from La Reunion Island), 42 (28%) came from Asia, 21 (14%) from Africa (16 from West Africa, four from Central Africa and one from East Africa) and 16 (11%) from South America and the Caribbean. Imported cases from Asia, 21 (14%) from Africa (16 from West Africa, four from Central Africa and one from East Africa) and 16 (11%) from South America and the Caribbean decreased in 2008 as compared with 2006–2007 (Figure 1).

Among the 16 imported cases from West Africa (Figure 2), seven came from
**Figure 1:** Mandatory notification of imported dengue cases to metropolitan France from July 2006 to December 2008, classified by region and year of acquisition

<table>
<thead>
<tr>
<th>Year</th>
<th>South America &amp; Caribbean</th>
<th>Africa</th>
<th>Asia</th>
<th>French Overseas Territories</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006 (n=30)</td>
<td>13%</td>
<td>10%</td>
<td>50%</td>
<td>13%</td>
</tr>
<tr>
<td>2007 (n=56)</td>
<td>13%</td>
<td>9%</td>
<td>61%</td>
<td>8%</td>
</tr>
<tr>
<td>2008 (n=62)</td>
<td>8%</td>
<td>21%</td>
<td>32%</td>
<td>39%</td>
</tr>
</tbody>
</table>

**Figure 2:** Imported dengue cases from West African countries to metropolitan France notified from July 2006 to December 2008

- Mali: 3 (2008)
- Togo: 1 (2008)
Côte d’Ivoire, four from Burkina Faso, three from Mali, two from Senegal and one from Togo (one of these patients returned from a trip to Mali and Côte d’Ivoire); one case was reported in 2006, three cases in 2007 and 12 cases in 2008, a 300% increase in 2008 compared with 2006–2007. The six patients returning from Côte d’Ivoire in 2008 were individually contacted to document the places visited during their stay in that country. During the 15 days before the onset of symptoms, corresponding to the maximal incubation period, four of the six patients stayed exclusively in Abidjan whereas the remaining two stayed in Abidjan and Grand-Bassam, located along the coast at about 40 km from Abidjan.

The number and the proportion of patients returning from Côte d’Ivoire increased significantly in 2008 compared with the previous 18 months. The increase was not statistically significant considering the patients returning from West African countries other than Côte d’Ivoire (Table 1). Data from the French Civil Aviation Authority show a relative stability in the number of air travellers between France and the West African countries where dengue cases were imported (+4.3% in 2008 compared with 2006–2007, see Figure 3) and an increase of 20.0% in air travellers between France and Côte d’Ivoire in 2008 compared with 2006–2007. This slight increase in air travel does not explain the high increase observed in imported dengue cases to France (Table 1).

Baseline characteristics of the patients in terms of sex and age were similar in patients from West African countries when compared

**Figure 3:** Quarterly number of imported dengue cases from West African countries to France (bars) and quarterly number of air travellers between West African countries and France (curve), July 2006 – December 2008

West African countries with imported dengue cases include Burkina Faso, Côte d’Ivoire, Mali, Senegal and Togo. Air travellers are from or to these West African countries. (Source for air travellers: French Civil Aviation Authority, 2009)
**Table 1:** Mandatory notification of imported dengue cases to metropolitan France from July 2006 to December 2008, according to the period of acquisition

<table>
<thead>
<tr>
<th>Period of acquisition</th>
<th>No. cases in the countries of travela</th>
<th>Total of imported cases (%)</th>
<th>Number of air travellersb</th>
<th>P-valuec</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Côte d’Ivoire</td>
<td>West Africa excluding Côte</td>
<td>Côte d’Ivoire</td>
<td>West Africa excluding Côte</td>
</tr>
<tr>
<td></td>
<td></td>
<td>d’Ivoire</td>
<td></td>
<td>d’Ivoire</td>
</tr>
<tr>
<td>Jul. 2006 – Dec. 2007</td>
<td>1/86 (1.1)</td>
<td>3/86 (3.5)</td>
<td>1/248 854</td>
<td>3/1 348 514</td>
</tr>
<tr>
<td>P-value</td>
<td>0.022</td>
<td>0.11</td>
<td>0.033</td>
<td>0.10</td>
</tr>
</tbody>
</table>

aWest African countries with imported dengue cases include Burkina Faso, Côte d’Ivoire, Mali, Senegal and Togo.
bAir travellers from or to the West African countries listed above.
cComparison of percentages between the two periods by Fisher’s exact test or Chi-square test.
(Source for air travellers: French Civil Aviation Authority, 2009)

with patients returning from other countries. Pain, particularly arthralgia, was significantly less frequent in patients returning from West African countries. Signs of severity (haemorrhage, thrombocytopenia) seemed less frequent in patients returning from WAC, but the difference between the two groups did not reach statistical significance. Finally, two third of the patients were hospitalized (Table 2).

Although biological diagnosis was performed either by PCR or by serology, dengue serotype determination by RT-PCR was only performed in three patients from WAC. DENV-1 was isolated in a patient from Burkina Faso in 2007, and DENV-3 was isolated in two patients from Côte d’Ivoire in 2008. For one of the DENV-3-infected patients returning to France in June 2008, data from the gene sequence of the protein E (GenBank accession no. FM213456) showed that this isolate presented a very strong identity (99.6%) with the sequence of the Japanese patient isolate.[9] A phylogenetic analysis limited to this region of the genome has shown that these two isolates are very likely related (an average of 99.2% identity) to the 2004 Saudi Arabia DENV-3 strain.

**Discussion**

There is a possible limitation to our study: we have no information on the completeness of the mandatory notification, which may be low in France, particularly during the first months after its introduction in 2006. The high proportion of hospital admissions may reflect better participation of hospital physicians compared with general practitioners. The lack of completeness, however, is probably not linked to the country of acquisition; if there is incomplete notification then it is regarding the overall number of dengue cases imported to France, which may be underestimated.

Several factors contribute to an underestimation of the disease burden due to dengue infection in West Africa. Firstly,
Dengue fever imported from West Africa to France

Table 2: Dengue patient’s characteristics according to the place of acquisition, July 2006–December 2008

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Place of travel</th>
<th></th>
<th>P-valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>West Africaa n=16</td>
<td>Elsewhere n=132</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>56.3%</td>
<td>47.7%</td>
<td>0.52</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>51 years (19-71)</td>
<td>41 years (7-67)</td>
<td>0.29</td>
</tr>
<tr>
<td>Pain</td>
<td>87.5%</td>
<td>99.2%</td>
<td>0.03</td>
</tr>
<tr>
<td>Myalgia</td>
<td>53.8%</td>
<td>62.7%</td>
<td>0.37</td>
</tr>
<tr>
<td>Headache</td>
<td>30.8%</td>
<td>49.1%</td>
<td>0.21</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>7.7%</td>
<td>40.0%</td>
<td>0.02</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>15.4%</td>
<td>7.3%</td>
<td>0.29</td>
</tr>
<tr>
<td>Minor haemorrhagic symptoms</td>
<td>12.5%</td>
<td>28.7%</td>
<td>0.14</td>
</tr>
<tr>
<td>Major haemorrhagic symptoms</td>
<td>0.0%</td>
<td>2.6%</td>
<td>0.69</td>
</tr>
<tr>
<td>Platelets ≤100,000/mL</td>
<td>26.7%</td>
<td>49.2%</td>
<td>0.10</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>75.0%</td>
<td>61.3%</td>
<td>0.29</td>
</tr>
</tbody>
</table>

aWest African countries with imported dengue cases include Burkina Faso, Côte d’Ivoire, Mali, Senegal and Togo.
bComparison of percentages between the two periods by Fisher’s exact test or Chi-square test; bold face represents a statistically significant result (P<0.05).

Disease surveillance data and systems are often lacking. Furthermore, limited access to health care may hinder the detection of symptomatic cases in West African countries. Finally, dengue infection diagnosis is difficult as it is often asymptomatic, and misdiagnoses are frequent because symptoms are non-specific and severe forms infrequent among imported cases, as suggested by a low frequency of haemorrhagic forms reported in our study, and tests are not widely available.

Surveillance of imported cases of infectious diseases among travellers to developed countries can be used for the early detection of epidemic activity in specific areas, as shown by our study and other published studies.14,15 Despite probable incompleteness, the mandatory notification surveillance system in France allows monitoring the trends of imported dengue cases from countries worldwide, especially those which lack surveillance systems for dengue.

Since the beginning of 2008, dengue cases imported from West Africa, particularly from Côte d’Ivoire, are increasing. We conclude that this is due to increased dengue circulation in this area. This information was shared with the World Health Organization and local authorities, resulting in an investigation in Abidjan by the Global Outbreak Alert and Response Network. This investigation confirmed the emerging of DENV-3 and led
to the transfer of technology for laboratory diagnosis in Abidjan.[16]

The introduction of a new serotype may cause important epidemics and be associated with a higher proportion of severe forms in case of secondary dengue, i.e. sequential infection with two serotypes. This may especially be true because DENV-3 has previously been associated with high-severity outbreaks in many countries[11] and because it was isolated in the few severe forms ever reported in Africa.[13] These data have public health implications for epidemiological surveillance and management of patients locally. Further study is needed on the epidemiology and seasonal patterns of the four dengue serotypes in West African countries.[14]

Acknowledgements

We are indebted to Philippe Barboza, Sandra Cohuet and Philippe Després for reviewing the manuscript, and to Nicolas Berthet for his technical assistance in conducting typing of the dengue strain. We thank the physicians for providing the mandatory notification.

References


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