DIAGNOSIS OF MALARIA IN NON-ENDEMIC COUNTRIES BY THE PARASIGHT-F® TEST

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Abstract. QBC®, examination of thin blood smears, and Parasight-F® were performed for every case of malaria suspected between May 1997 and December 1998. Data from 310 patients were reported. Fifty had malaria infection diagnosed by QBC® and thin blood film, among whom 39 had Plasmodium falciparum infection. Three of these 39 were negative with the Parasight-F® test. Eleven patients had a positive Parasight-F® test but microscopic diagnosis methods were negative. Interpretation of these 11 positive Parasight-F® results is proposed to depend on clinical criteria.

INTRODUCTION

In non-endemic areas, diagnosis of imported malaria on the basis of microscopic examination remains the major diagnostic method. However, interpretation of thick and thin blood smears requires trained microscopists and, for the QBC® method (Becton Dickinson, Meylan, France), specific and relatively expensive equipment (fluorescence microscope and specific kits). Newer methods based on detection in blood of a soluble glycoprotein specific to Plasmodium falciparum, the histidine rich protein-II (HRP-II), have been developed.1–3 These commercially available tests do not require specific equipment and are rapid and simple to perform. Their sensitivity and specificity are near 90% but vary in different studies.1,2,4,5 To estimate the impact of the Parasight-F® test (Becton Dickinson) on malaria diagnosis in a clinical laboratory, we retrospectively analyzed the discrepancy between Parasight-F® test results and conventional diagnostic methods according to the clinical course and final clinical diagnosis of patients in Grenoble, France.

MATERIALS AND METHODS

For each case of suspected malaria seen between May 1997 and December 1998, at Grenoble University Hospital, QBC®, examination of thin blood smear, and Parasight-F® test were performed. Species identification and intensity of parasitemia were determined on thin blood smears. Parasitemia was expressed as the percentage of infected erythrocytes. Data from 310 patients were analyzed. These febrile patients were French travelers returning from malarial endemic areas or immigrants from endemic areas, mainly Africa. Clinical information was collected. Rheumatoid factor and anti-nuclear antibody were measured when discordance was observed between QBC®/thin blood smear and antigen detection by the Parasight-F® test. Sensitivity, specificity and predictive values were calculated using microscopy as the reference method.

RESULTS

Fifty of 310 patients had malaria infection according to positive parasite detection by QBC® and thin blood film examination. Thirty-eight had P. falciparum (35 positive with Parasight-F®), one mixed infection with P. falciparum and Plasmodium ovale (positive with Parasight-F®) and 11 with other species (seven P. ovale and four P. vivax; all were negative with Parasight-F®).

Accordingly, antigen detection resulted in three false-negative results. One of these patients had only sexual forms of P. falciparum, and the other two had P. falciparum trophozoites with parasitemia < 0.01%. During the follow-up of one of these two cases, the Parasight-F® test became positive two days after diagnosis and treatment with halofantrine whereas the microscopic examination became negative.

For 11 patients, the Parasight-F® was positive and the QBC® and thin smear were negative. These results are summarized in Table 1. They show that: 1) for three patients, positive Parasight-F® test was present when the subjects were empirically treated with anti-malarial drugs for several days before diagnosis (cases 3 to 5); 2) for six patients, the interpretation of the Parasight-F® test was equivocal and it was not possible to determine if this corresponded to true malaria infection (cases 6 to 11). Another diagnosis was made in five of these patients and only one was treated despite the absence of positive antigenemia in repeated blood samples. Three of these patients had previously received chemoprophylaxis with chloroquine and proguanil association or mefloquine during their stay in endemic areas. And 3) Two positive Parasight-F® tests were false-positive. The first patient had not traveled in a malarial endemic area (the West Indies) and the rheumatoid factor level was high. The final diagnosis for the second patient was a primary cytomegalovirus infection. The Parasight-F® test was not consistently positive in this group.

Overall, the sensitivity and specificity of the Parasight-F® test were 92.3% and 95.9% compared with QBC® and microscopy, respectively. The positive and negative predictive values were 76.5% and 98.8%, respectively. If the three cases with persistent antigenemia were not considered false-positive, despite negative microscopy, the sensitivity and specificity of the Parasight-F® test were 92.8% and 97%. The positive and negative predictive values were 82.9% and 98.8%.

DISCUSSION

This retrospective analysis adds to our understanding of the Parasight-F® test in non-endemic areas. In spite of the
**Table 1**

Description of the 11 patients with positive ParaSight-F/H23041 and negative microscopic examination.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Treatment on different blood samples</th>
<th>Final clinical diagnosis</th>
<th>RF/AA Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (West Indies)</td>
<td>No</td>
<td>1/1</td>
<td>Pyelonephritis</td>
</tr>
<tr>
<td>2 (Vietnam)</td>
<td>ND</td>
<td>2/4</td>
<td>CMV primary infection</td>
</tr>
<tr>
<td>3 (Ivory Coast)</td>
<td>No</td>
<td>1/1</td>
<td>Malaria</td>
</tr>
<tr>
<td>4 (Benin)</td>
<td>Paludrine/H11001</td>
<td>1/1</td>
<td>Malaria</td>
</tr>
<tr>
<td>5 (Senegal)</td>
<td>Paludrine/H11001</td>
<td>1/1</td>
<td>Probable malaria</td>
</tr>
<tr>
<td>6 (Vietnam)</td>
<td>Mefloquine</td>
<td>1/3</td>
<td>Fever of unknown origin</td>
</tr>
<tr>
<td>7 (Benin)</td>
<td>Paludrine/H11001</td>
<td>1/1</td>
<td>Schistosomiasis</td>
</tr>
<tr>
<td>8 (Tanzania)</td>
<td>Mefloquine</td>
<td>1/1</td>
<td>Appyretic, macular eruption</td>
</tr>
<tr>
<td>9 (Mali)</td>
<td>ND</td>
<td>1/1</td>
<td>Peritonitis, appendectomy</td>
</tr>
<tr>
<td>10 (Ivory Coast)</td>
<td>ND</td>
<td>1/1</td>
<td>Hepatic encephalopathy, delirium tremens</td>
</tr>
<tr>
<td>11 (Antecedent of malaria, Guinea)</td>
<td>ND</td>
<td>1/1</td>
<td>Hepatic encephalopathy, dementia</td>
</tr>
</tbody>
</table>

**Interpretation**

- 280/Neg: 280 copies/mL of HRP-II in the test.
- ND: Not done.
- Neg: Negative result.
- Positivity: Positive result.
- 40/Neg: 40 copies/mL of HRP-II in the test.

*RF*: rheumatoid factor; *AA*: antinuclear antibody; *Ag*: antigenemia; *ND*: not done; *CMV*: cytomegalovirus.

**Acknowledgments:** We thank S. Durville for English proofreading.
REFERENCES


