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Correspondence

Suboptimal diagnostic performance of dengue non-structural protein 1 antigen rapid test during non-endemic periods in southern Taiwan

Dear Editor,

Dengue caused major outbreaks in southern Taiwan. Laboratory diagnosis is consistently required to distinguish dengue from other febrile illness causing similar clinical presentations.[1] The detection of non-structural protein 1 (NS1) antigen in patients' serum can support the diagnosis as early as the first day of disease onset and remain positive during the first week.[2] Therefore, NS1 antigen detected by rapid immunochromatographic assays had been used widely in endemic settings with acceptable sensitivity and specificity.[3]

Physicians in Taiwan incorporated dengue NS1 antigen rapid tests into clinical practice during the 2015 epidemic. In the following years, rapid tests were applied to the sporadic suspected cases of dengue fever. This provided us an opportunity to assess the performance of the test during non-endemic periods.

We retrieved all patients tested either by SD BIOLINE Dengue Duo or SD BIOLINE Dengue NS1 Ag rapid test (Standard Diagnostics, Yongin, Korea) at National Cheng Kung University Hospital between January 01, 2016 and December 31, 2017. The cases of positive results were identified. Their medical records and testing results from the reference laboratory of Taiwan Centers for Disease Control were reviewed. The diagnosis of dengue is established by a positive result of nucleic acid amplification or serological evidences (including seroconversion or a four-fold or greater rise in serum dengue-specific immunoglobulin G titers).

Among 1262 non-duplicated patients tested by the NS1 antigen rapid test, sixteen (1.27%) had positive results. Nine of the 16 patients had confirmed dengue, while seven were regarded to have false-positive rapid test results, indicating a positive predictive value of 56.3% (9/16). With the exclusion of six febrile patients with a recent travel history to dengue-endemic countries (3 Philippines and 3 Vietnam), the false-positive rate rose from 43.8% (7/16) to 70.0% (7/10). These patients with false-positive rapid test results had different acute illness with or without underlying systemic diseases (Table 1), and of them three presented with septic shock. In contrast, none of those with dengue evolved into dengue shock. Among three patients without recent travel history, hospital-onset dengue developed in two adults on the 19th and 24th day, respectively, after receiving renal transplant from the same deceased donor.

False positive results of serum dengue NS1 antigen rapid tests had been described, but was limited to very few cases reporting the association of false positivity and hematological diseases or Zika virus infection.[4,5] In the current study, acute illness associated with false-positivity included bacterial or viral infections and non-infectious diseases, precluding us from attributing such false-positive results to specific acute or chronic illness.

Physicians in Taiwan should be aware that during a non-endemic period, the pretest probability is too low that the positive predictive value of the serum dengue NS1 antigen rapid test remains suboptimal to establish the diagnosis of dengue, especially for individuals without recent travel to endemic areas. Without local dengue endemics, a patient with a positive result of NS1 rapid test may not be managed as dengue viral infection, and the possibility of other infectious diseases should be kept in mind.

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Table 1 Clinical diagnosis of seven patients with false-positive NS1 antigen rapid test results.

No.	Age/Sex	Acute illness	Chronic underlying diseases
1	37y/M	Septic shock and Lemierre's syndrome with *Fusobacteirum necrophorum* bacteremia	Renal lithiasis
2	58y/M	Septic shock, spondylodiskitis and psoas muscle abscess with MRSA[a] bacteremia	Spinal cord injury, end-stage renal disease, gallstones
3	10m/F	Roseolla infantum	nil
4	19y/M	Acute suppurative tonsillitis	nil
5	78y/F	Acute ischemic stroke	Adrenal insufficiency, peptic ulcer disease
6	65y/M	Scrub typhus	Hypertension, atrial fibrillation
7	85y/F	Influenza A(H3) with septic shock	Atrial fibrillation

[a] Methicillin-resistant *Staphylococcus aureus*.

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