Does negative IgM dengue serology rule out dengue fever in an adult with fever for three days?

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History

A 21-year old medical student consults the doctor for a fever that started 3 days ago. The fever was high grade and associated with generalised body aches. There was no gum bleeding. He mentioned that mosquito fogging was conducted in his neighbourhood recently.

Physical examination revealed an alert conscious young man. Temperature (oral): 38.9°C, blood pressure 100/70 mmHg, pulse rate 90/min, good volume. Mild flushing was noted. No petechiae were seen in his legs. Tourniquet test was positive.

Investigations

Full blood count: packed cell volume 45%, total white 1.7×10^9/L, platelet 87×10^9/L. Dengue IgM and dengue IgG serology were negative.

Clinical question

Does negative IgM dengue serology rule out dengue fever in an adult with fever for three days?

EBM in PICO format:

Patient	Adult with acute fever for 3 days
Index test	IgM dengue serology
Comparison test	Dengue virus isolation or polymerase chain reaction
Outcome	Dengue fever

Discussion

In answering the clinical question, we searched the PubMed for literature using combination of the following MeSH terms: dengue, diagnosis, immunoglobulin M, sensitivity and specificity (number of items =145). We also added "systematic review, meta-analysis, Asia" in various combinations to identify publications closely relevant to our question and clinical setting.

Acute fever is a distressing symptom and fear of sinister causes often results in early presentation in primary care. Although the majority are caused by self-limiting illness, serious infective causes of fever are always lurking in the mind of the primary care doctors. In the Malaysian context, dengue fever is high on the differential diagnosis list if there is no obvious localizing clinical feature.

Clinical features (high fever, retro-orbital pain, malaise, arthralgia, flushing, and "islands of white in a sea of red") and full blood count abnormalities (leucopenia, thrombocytopenia) of dengue fever overlap considerably with other viral infections. Tanner et al derived a dengue diagnostic algorithm incorporating many of these simple clinical and haematological parameters.[1] Using this decision algorithm (incorporating thrombocytopaenia, leucopaenia and fever) would have placed our patient in the "probable dengue" category.

Blacksell et al conducted a meta-analysis of 11 studies evaluating dengue IgM.[2] The sensitivity and specificity of "early acute" samples (fever up to 7 days) were 73% and 88%, and "late acute" samples (fever 7-10 days) were 96% and 90%, respectively.[2] This study shows that dengue IgM performs best if it is done at the convalescent phase of dengue fever. The study findings do not fully address the clinical question raised in

the above case scenario (the patient's dengue serology was done on day 3 of fever). On the other hand, a study of 157 hospitalized febrile patients in Cambodia reported sensitivities of NS1 Ag test and IgM/IgG at Day 1-2 fever were 80% and 40% respectively, while at day 5-6, the corresponding figures were 40% and 84%.[3] A multi-centre study evaluating two commercial test kits for early diagnosis of dengue reported NS1 Ag test had a sensitivity of around 70% (combination of two tests) at Day 3 of illness.[3] In this study, it was shown that 71% IgM-negative dengue patients at day 3 had positive NS1 Ag test.[3]

In conclusion, dengue IgM serology has low sensitivity during the early phase of dengue fever. Negative IgM cannot rule out dengue fever. NS1 Ag test is the preferred diagnostic test in the above patient. We noted, however, that the decision whether to pursue immunological testing in the above patient has cost implication as such tests are much more expensive than the usual full blood count. In a resource poor setting, it may be appropriate to manage the above patient as dengue using basic haematological tests rather than pursuing serological tests.

How does this paper make a difference to general practice

Laboratory tests (other than full blood count) are seldom performed for patients with suspected dengue fever in primary care. This Journal club highlights the value of definitive dengue diagnostic tests, in particular NS1 antigen test, in the early phase of dengue fever.

References

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