Use of the Xpert MTB/RIF assay in the diagnosis of tuberculous meningitis: A cautionary note

To the Editor: The Xpert MTB/RIF (Cepheid) assay is a nucleic acid amplification test developed to detect mycobacterial tuberculosis (MTB) infection and rifampicin resistance. It is a closed system, requires minimal training to use, and produces a result in a few hours. When used as an initial diagnostic test replacing smear microscopy for pulmonary tuberculosis, the Xpert MTB/RIF has a pooled sensitivity of 88%. The application of this test has been extended to extrapulmonary samples, including cerebrospinal fluid (CSF).

The World Health Organization (WHO) evaluated the results of 709 CSF samples tested with Xpert MTB/RIF in 16 studies using culture as a reference standard. Sensitivity varied widely, ranging from 51% to 100%. Using a 3 ml volume of CSF and including a concentration step increased sensitivity.

The WHO recommends that the Xpert MTB/RIF should be the first test to be undertaken on CSF from patients with suspected tuberculous meningitis (TBM). However, caution is advised, as the following case illustrates.

A 43-year-old HIV-positive man was admitted to a peripheral hospital in South Africa with a 2-week history of headache and a more recent onset of slurred speech, inability to walk and impaired consciousness. A computed tomography scan of the brain showed mild hydrocephalus and basal enhancement. Lumbar puncture revealed an opening pressure of 4 cm H2O, yellow colour, lymphocytes 300/l, a protein level of 1.06 g/l and glucose level of 1.3 mmol/l. The Xpert MTB/RIF was negative. On the basis of this negative test result, initiation of antituberculosis (anti-TB) therapy was deferred and ceftriaxone was started. The patient was referred to the neurology unit at Inkosi Albert Luthuli Central Hospital in Durban 4 days later. He was noted to have a Glasgow Coma Score of 8/15, meningism and normal optic fundi. He could move all his limbs. Anti-TB drugs and steroids were commenced, but he died within 3 hours of admission.

Ignoring the Xpert MTB/RIF result, this patient’s clinical, radiological and CSF profile is consistent with probable TBM. As standard of care, he would have been started on anti-TB therapy and steroids while awaiting the other laboratory results.

The Xpert MTB/RIF test should be subjected to post-WHO recommendation scrutiny to determine how well it performs in routine clinical practice for the diagnosis of TBM.

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