1703. Delta-like 1 ligand (DLL) measurement in cerebrospinal fluid for detection of *Mycobacterium tuberculosis* meningitis

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Background. Tuberculosis meningitis (TBM) diagnosis is notoriously difficult, new biomarkers are needed to allow for improved diagnostic accuracy. We evaluated the diagnostic utility of a novel biomarker, delta-like ligand 1 (DLL1), a Notch ligand, which selectively drives antigen-specific CD4 T helper1 cell responses. DLL1 polymorphisms increase susceptibility to other intraceullar (Th1) organisms (e.g., leishmaniasis).

Methods. CSF DLL1 concentrations were measured by ELISA in 116 patients with suspected meningitis, of which 18 patients had TBM, 65 patients cryptococcal meningitis (CM), and 33 patients tested negative for both CM and TBM (termed "other"). TBM was diagnosed either by GeneXpert MTB/Rif assay (Cepheid, Sunnyvale, CA) or Bactec MGIT culture. We evaluated the diagnostic performance of DLL1 for TBM.

Results. Patient characteristics were similar at diagnosis except for CSF protein and CSF WBC count. Protein was higher in TBM patients than 'other' meningitis, and CSF WBC count, was higher in TBM than in non-TBM meningitis. Mean DLL1 CSF concentrations were significantly higher in patients with TBM (1293 pg/mL; 95%CI, 602-1985 pg/mL) than CM (447 pg/mL; 95%CI, 398-495pg/mL) or other meningitis (534 pg/mL; 95%CI, 290-669pg/mL). A cutoff of >600pg/mL in CSF for TBM had 72% sensitivity, 77% specificity, 36% positive predictive value (PPV), and 94% negative predictive value (NPV) 94% (AUC = 0.794). As the DLL1 level increased, the likelihood of TBM increased with specificity of 92% and PPV of 56% above >800pg/mL.

Conclusion. CSF DLL1 exhibited good diagnostic performance, and may have a role as a low cost adjunctive diagnostic tool for TBM. Misclassification bias (of non-detection of TBM classified as 'other') hampers diagnostic studies, and larger studies are required in the future.

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