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Clinical aspects

Agreement between local and central anti-synthetase antibodies detection: results from the Classification Criteria of Anti-Synthetase Syndrome project biobank

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Abstract

OBJECTIVES:

The CLASS (Classification Criteria of Anti-Synthetase Syndrome) project is a large international multicentre study that aims to create the first data-driven anti-synthetase syndrome (ASSD) classification criteria. Identifying anti-aminoacyl tRNA synthetase antibodies (anti-ARS) is crucial for diagnosis, and several commercial immunoassays are now available for this purpose. However, using these assays risks yielding false-positive or false-negative results, potentially leading to misdiagnosis. The established reference standard for detecting anti-ARS is immunoprecipitation (IP), typically employed in research rather than routine autoantibody testing. We gathered samples from participating centers and results from local anti-ARS testing. As an “ad-interim” study within the CLASS project, we aimed to assess how local immunoassays perform in real-world settings compared to our central definition of anti-ARS positivity.

METHODS:

We collected 787 serum samples from participating centres for the CLASS project and their local anti-ARS test results. These samples underwent initial central testing using RNA-IP. Following this, the specificity of ARS was reconfirmed centrally through ELISA, line-blot assay (LIA), and, in cases of conflicting results, protein-IP. The sensitivity, specificity, positive likelihood ratio and positive and negative predictive values were evaluated. We also calculated the inter-rater agreement between central and local results using a weighted κ co-efficient.

RESULTS:

Our analysis demonstrates that local, real-world detection of anti-Jo1 is reliable with high sensitivity and specificity with a very good level of agreement with our central definition of anti-Jo1 antibody positivity. However, the agreement between local immunoassay and central determination of anti-non-Jo1 antibodies varied, especially among results obtained using local LIA, ELISA and “other” methods.

CONCLUSIONS:

Our study evaluates the performance of real-world identification of anti-synthetase antibodies in a large cohort of multi-national patients with ASSD and controls. Our analysis reinforces the reliability of real-world anti-Jo1 detection methods. In contrast,

challenges persist for anti-non-Jo1 identification, particularly anti-PL7 and rarer antibodies such as anti-OJ/KS. Clinicians should exercise caution when interpreting anti-synthetase antibodies, especially when commercial immunoassays test positive for non-anti-Jo1 antibodies.

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