SPOT ON! EVALUATION OF T-SPOT.TB FOLLOWING INDETERMINANT QUANTIFERON TB-GOLD PLUS IN SCREENING FOR LATENT TUBERCULOSIS

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Background: Current guidelines recommend screening for latent tuberculosis in at risk patients, including immunosuppressed patients, particularly those receiving anti-TNF-alpha therapy.¹ Interferon- γ release assays (IGRA), including T-SPOT.TB (TS) and QuantiFERON TB-Gold Plus (QFG), are one method for case identification. Our lab suggests requesting TS after indeterminate QFG, although evidence for this approach is limited.¹

Methods: A retrospective audit of TS tests from November 2018 to October 2019 was performed to identify the results of testing after indeterminate QFG. Additional details, including QFG mitogen response, source of referral, and interval between QFG and TS, were also examined.

Results: Eighty TS tests with a history of indeterminate QFG result were identified. Seventy-two (90%) had a clear result, with the majority being negative (69 tests, 86%) and three positive results (3.8%). Of the remaining requests four (5%) were not performed due to low cell counts, three (3.8%) had an indeterminate result, and one (1.8%) was uninterpretable due to high background.

Discussion: Our current strategy utilising a second IGRA (TS) after indeterminate QFG led to clarification of indeterminate results in the vast majority (90%) of cases. This outcome supports continuing our testing strategy and provides some evidence to inform changes to guidelines.

Reference

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DEMONSTRATION OF ECULIZUMAB DEPOSITION BY DIRECT IMMUNOFLUORESCENCE ON A RENAL BIOPSY IN A CASE OF ATYPICAL HAEMOLYTIC URAEMIC SYNDROME

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Ecilizumab is an IgG2/IgG4 kappa monoclonal antibody that blocks C5 and subsequent terminal complement pathway activation. It can be useful in complement-mediated atypical haemolytic uraemic syndrome occurring as a consequence of complement dysregulation. We report a case demonstrating

direct immunofluorescence (DIF) findings suggestive of ecilizumab binding to renal tissue.

A 40-year-old man with primary focal segmental glomerulosclerosis underwent deceased donor renal transplantation. After an unremarkable post-transplant period, he developed thrombotic microangiopathy (TMA) complicated by graft dysfunction and ischaemic ileal ulcers. Despite commencing ecilizumab for possible complement-mediated aHUS, he had progressive renal impairment and persistent haematological features of TMA, and proceeded to graft nephrectomy five days post-ecilizumab administration. On DIF, renal tissue demonstrated sparse focal lobular aggregates of IgG within glomeruli and bright IgG deposition within walls of tubules, which was kappa light-chain restricted. Serum free light chain ratio was normal, and no serum paraprotein was detected. Renal biopsies pre-ecilizumab administration did not demonstrate this binding pattern. Further examination revealed IgG2 and IgG4 subclass restriction, suggestive of ecilizumab binding to C5 in renal tissue. Similar renal biopsy staining patterns have been attributed to ecilizumab deposition.^{1,2} Pathologists should be aware that therapeutic monoclonal antibodies may be detected on biopsy specimens.

References

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2. Singh P, Chen H, Gordon CE, *et al.* Monoclonal IgG4/2 κ deposition following ecilizumab therapy for recurrent atypical hemolytic uremic syndrome in kidney transplantation. *Kidney Med* 2019; 1: 139–43.

HEPATITIS C-ASSOCIATED GLOMERULONEPHRITIS MASQUERADING AS GOODPASTURE'S SYNDROME

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Anti-glomerular basement membrane (GBM) autoantibodies are associated with Goodpasture's syndrome, characterised by lung and kidney involvement. We report a case with clinical disease demonstrating discrepant anti-GBM antibody results between assay platforms.

A 39-year-old male presented with an eight-week history of haemoptysis and acute renal impairment, on a background of active hepatitis C infection. Creatinine was 256 μ mol/L with haemoproteinuria, hypocomplementaemia, and positive anti-GBM level (65 U/mL Phadia ELiA; reference range >10 U/mL) which was confirmed on repeat testing. Treatment for Goodpasture's syndrome was initiated with plasma exchange (PLEX) and intravenous cyclophosphamide. However, renal biopsy performed in parallel to treatment did not demonstrate characteristic linear GBM binding on direct immunofluorescence. Findings were instead consistent with hepatitis C-associated glomerulonephritis. ANCA by immunofluorescence was negative. Anti-PR3, anti-MPO and anti-CCP tested retrospectively by Phadia ELiA methods were also positive, raising suspicion for an interfering factor. Pre-treatment sera tested for anti-GBM antibodies via indirect immunofluorescence (INOVA primate kidney) and chemiluminescence assay (INOVA BIO-FLASH)