2025 Pathology Update

C5N1A Antibody Testing – How Are We Travelling?

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BACKGROUND:

Inclusion body myositis (IBM) is a progressive inflammatory muscle disease that causes muscle wasting, resulting in reduced mobility, accumulation of disability and reduced quality of life (1,4). Historically, the diagnosis was established by muscle biopsy, with characteristic histology demonstrating CD8+ T cell and macrophage invasion of myofibres, rimmed vacuoles, multi-protein inclusion bodies, mitochondrial abnormalities and expression of major histocompatibility complex molecules (1). In 2011 antibodies against cytosolic 5'-nucleotidase 1A (C5N1A) were discovered (4). C5N1A antibodies are reported to occur in 33-76% of IBM patients (1,3). They can occur in other autoimmune and connective tissue diseases (3,4), but are seen in <5% of patients with other forms of myositis or neuromuscular disorders (4). The discovery of C5N1A antibodies has had significant implications for the investigation and diagnosis of IBM, with a reduction in the time to diagnosis, the need for diagnostic muscle biopsy and allowing a more personalized approach to management (3) .

The pathogenic role of C5N1A antibodies remains unclear, but the enzyme is known to catalyse the hydrolysis of nucleotides to nucleosides, which are abundant in skeletal muscles and aberrant in IBM muscles (1). Unlike other forms of myositis, no juvenile-onset form of the disease is recognized, with most cases affecting patients older than 45 years (4). IBM occurs more commonly in men than women and is not responsive to immunosuppression (3). The presence of C5N1A antibodies is also reported to be associated with a lower frequency of proximal upper-limb weakness at disease onset, an increased likelihood of facial weakness and an increased overall mortality (3,4).

C5N1A antibodies can be measured by western blot, enzyme linked immunosorbent assay (ELISA), immunoprecipitation with mass spectrometry, immunoblot (5, 6) and, more recently, by a cell-based immunofluorescence assay (6). PathWest Immunology have been performing an in house C5N1A antibody ELISA (2) since 2018, initially as a research assay and later as a NATA accredited assay.

AIM:

To review the sensitivity and specificity of the C5N1A assay and the clinical characteristics of C5N1A antibody positive patients in a WA cohort and compare to the published literature.

METHOD:

In the 37 months from August 2020 to September 2024 inclusive, samples from 841 patients were tested. Of those patients from WA (n=256), for which clinical information was available (n= 182), simple descriptive statistics were performed to evaluate assay sensitivity, specificity and patient clinical characteristics.

RESULTS:

- 841 patient results were reviewed
- Of the samples for which clinical information was available, 19.8% had a clinical diagnosis of IBM
- Assay sensitivity was 22.2%, specificity was 97.3%.

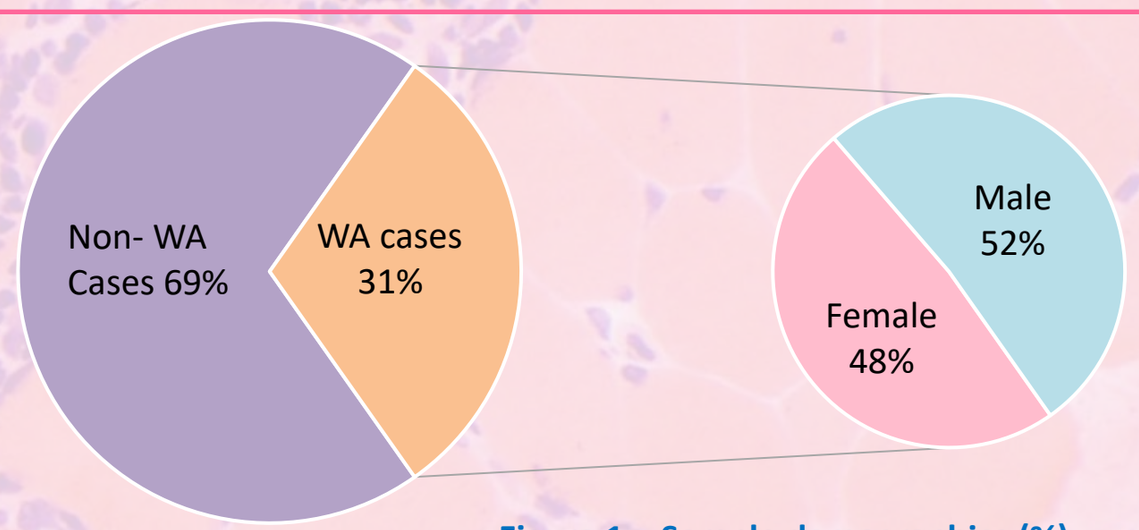

Figure 1 – Sample demographics (%)

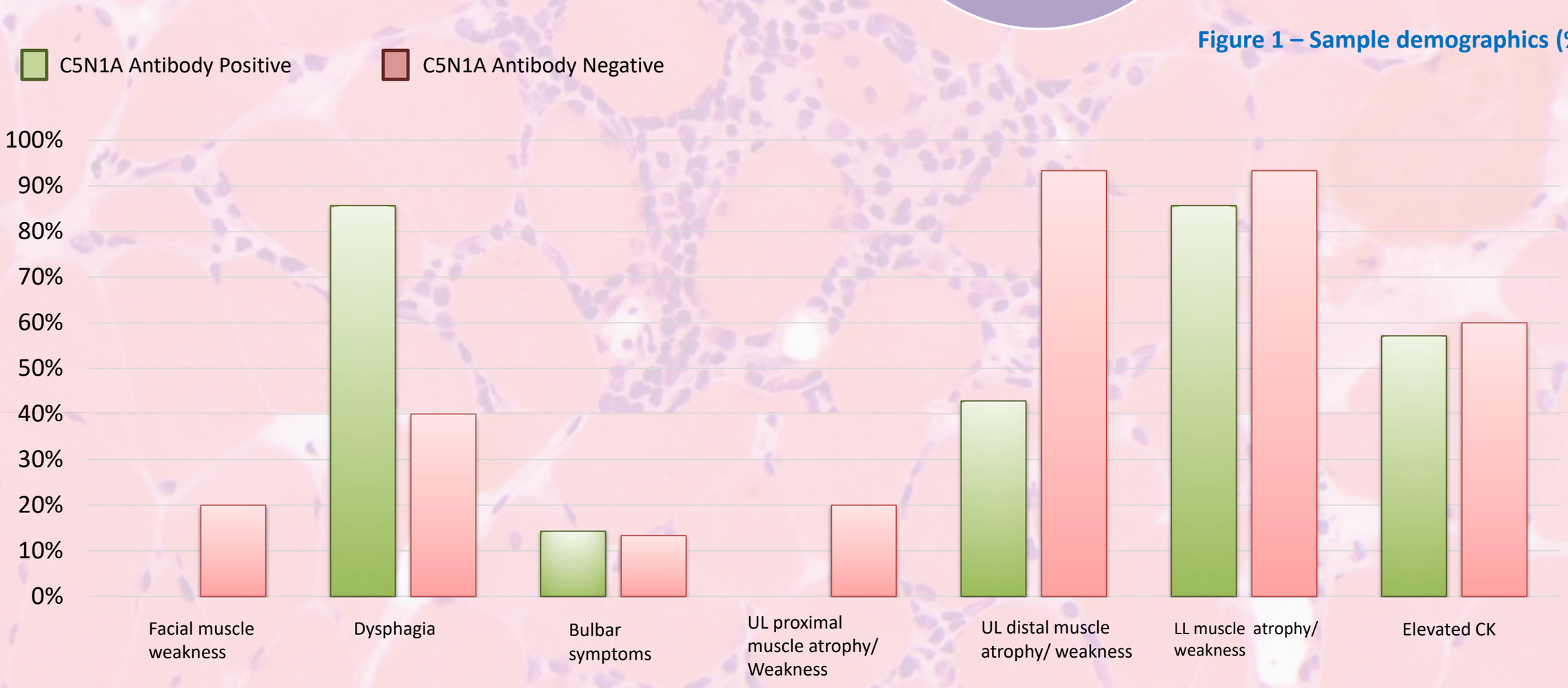

Figure 2 – Clinical characteristics of the confirmed IBM cases (UL = upper limb, LL = lower limb, CK = creatinine kinase)

CONCLUSION:

The WA experience with C5N1A antibody testing is relatively consistent with the literature. The assay sensitivity is slightly lower, and specificity higher, than that described, appreciating a very small sample size and limitations regarding clinical information. In our cohort, C5N1A antibody positive patients were more likely to have symptoms of dysphagia and less likely to have facial muscle weakness or upper limb muscle involvement at diagnosis (Figure 2).

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