Advancing Diagnostics: Exploring a Rapid Detection Method for Cryoglobulinemia

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What is Cryoglobulinemia?

Cryoglobulinemia is a rare condition, affecting approximately **1 in 100,000** globally, characterised by the presence of abnormal immunoglobulins (cyroglobulins) that precipitate **below 37°C** and resolubilise upon warming [1-4].

Brouet's Classification

Type	Immunoglobulin Composition	Cryoprecipitation Time
I	Monoclonal Ig (IgM, IgG, IgA)	< 24 h
II	Monoclonal IgM (RF+) + Polyclonal IgG	3–7 days
III	Polyclonal IgM (RF+) + Polyclonal IgG	≥ 3–7 days

Clinical Challenge

UKAS accredited process turnaround time (TAT) is variable due to dependence on cryoprecipitation rate.

Aim

Leverage physicochemical properties like isoelectric point and charge to accelerate detection of Type I/II cryoglobulinemia, reducing turnaround time (TAT) for timely clinical decisions.

Methods

6 potential cases were identified based on the following criteria:

- Change in immunoglobulin/paraprotein levels (>50% difference or fluctuation without treatment)
- Visual sample inspection ('cotton wool' like precipitate seen after incubation at 4°C
- Clotting issues flagged during biochemistry analysis

Detection Methodology

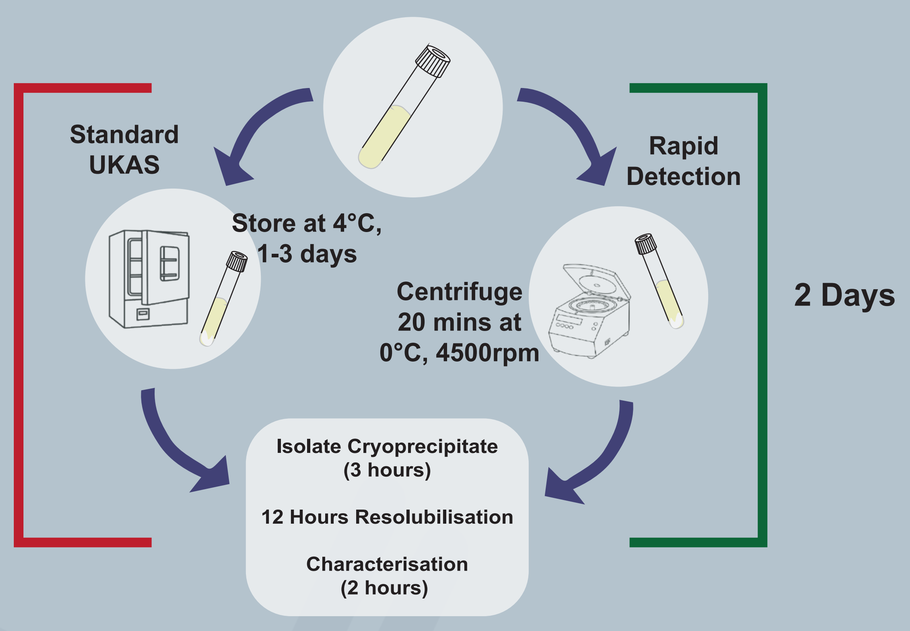

Figure 1. Flowchart showing difference in cold incubation period between UKAS accredited method and proposed rapid detection method

Confirmatory Testing

The 6 patients identified were subsequently called for confirmatory testing using the UKAS accredited cryoglobulin process.

Results

In the **6** cases identified a cryoprecipitate was observed in all after centrifugation which re-solubilised at 37°C, indicating presence of a cryglobulin.

Subsequent confirmatory testing classified 5 x Type I and 1 x Type II. All patients were not previously known to have cryoglobulinemia.

IgM was the most frequently detected isotype of the Type I cyroglobulinemias identified.

Type I Cryoglobunemia

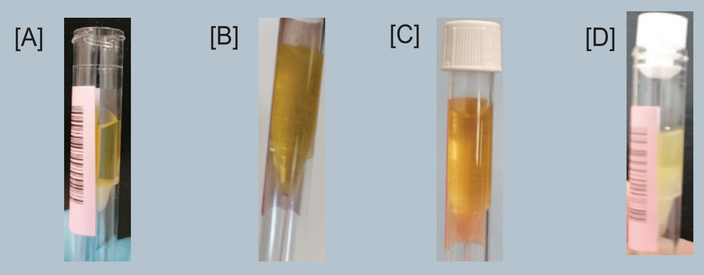

Figure 2. Rapid detection of type I cryoprecipitate using centrifuge for 20minutes at 0C. A) IgG Lambda B) IgM Kappa C) IgM Lambda D) IgM Kappa

Type II Cryoglobunemia

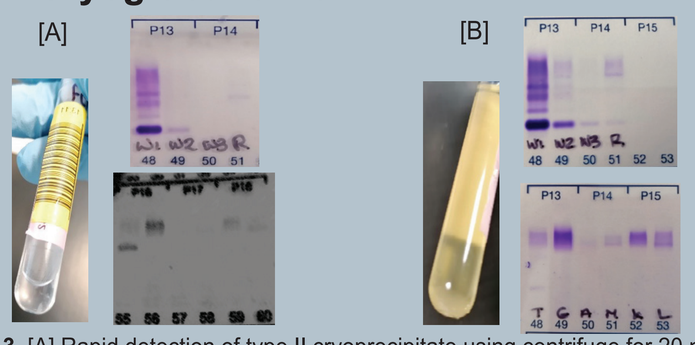

Figure 3. [A] Rapid detection of type II cryoprecipitate using centrifuge for 20 mins at 0°C. Wash with 4°C PBS. Immunofixation.[B] UKAS accredited detection of type II cryoprecipitate using centrifuge for 20 mins at 0°C. Wash with 4C PBS. Immunofixation.

The Type II cryoglobulinemia identified via the rapid detection method was a polyclonal IgG with a faint IgM Lambda, this was confirmed by the UKAS accredited cryoglobulin process.

Clinical Impact

Figure 4. [LEFT] IgM Kappa. a case of a patient with clinically unsuspected LPL identified because of sample viscosity

An 80-year-old female was scheduled for ED discharge when routine blood tests flagged errors due to a **viscous** sample.

A biomedical scientist's vigilance in recognising cryoglobulin formation prompted immediate investigation.

This led to a timely diagnosis of Waldenstrom's macroglobulinaemia, enabling expedited treatment and preventing future morbidity [5].

Conclusion

- Potential reduced turnaround time for result reporting
- Potential use as a screening tool for cryoglobulinemia in previously unknown samples that meet selection criteria.
- Further investigation required to validate for routine use in clinical laboratory practice.

References

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