Utility of routine use of an immunochemical panel (ELISA-4-Amyloid) for typing the four main types of systemic amyloidosis in fat tissue

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INTRODUCTION

Quick and reliable typing of amyloid is essential to prevent treatment delay. Extraction of amyloid from aspirated fat tissue enables immunochemical quantification by an enzyme-linked immunosorbent assay (ELISA) of the characterizing protein. ELISAs have been developed in our center for typing the 4 main types: AA, ATTR, AL-kappa, and AL-lambda amyloid.

OBJECTIVE

Aim of this study is to assess the diagnostic accuracy of the ELISA-4-amyloid panel in the routine setting of our daily clinical practice.

PATIENTS AND METHODS

Fat tissue aspirates of 912 patients and controls were studied: 105 AA, 130 ATTR, 85 AL-kappa, 212 AL-lambda patients and 380 controls. The amount of amyloid was graded in Congo red-stained specimens; 0 (no amyloid), 1+ (<1% of inspected area), 2+ (1-10%), 3+ (10-60%), 4+ (>60%). At least 30 mg of fat tissue was obtained per patient. A sandwich ELISA was used to quantify AA and indirect ELISAs were used to quantify ATTR, AL-kappa, and AL-lambda amyloid. The upper reference limits used (set 100%) were 11.6 (AA), 6.97 (ATTR), 1.41 (AL-kappa), and 1.71 ng/mg fat tissue (AL-lambda). A result higher than 100% was diagnostic for that type. If more than one protein was positive, the protein with the highest percentage was diagnostic for the type of amyloid.

RESULTS

Eight of the 318 non-amyloid controls were wrongly typed as amyloid. Three amyloid patients were wrongly typed as AA. Specificity of the ELISA-4-Amyloid panel is 98.8% (901/912). Seventy-five of 77 AA patients with grade 2+ and higher were identified (97%). Fifty-six of 58 ATTR patients with grade 3+ and 4+ were identified (97%). Thirty of 41 AL-kappa patients with grade 3+ and 4+ were identified (73%). One hundred and twenty of 147 AL-lambda patients with grade 3+ and 4+ were identified (82%). Sensitivity of typing of all Congo red-positive biopsies (1+ and higher) was highest in AA (91%, 90/99), followed by AL-lambda (69%, 140/204), ATTR (61%, 69/113), and AL-kappa (51%, 37/73).

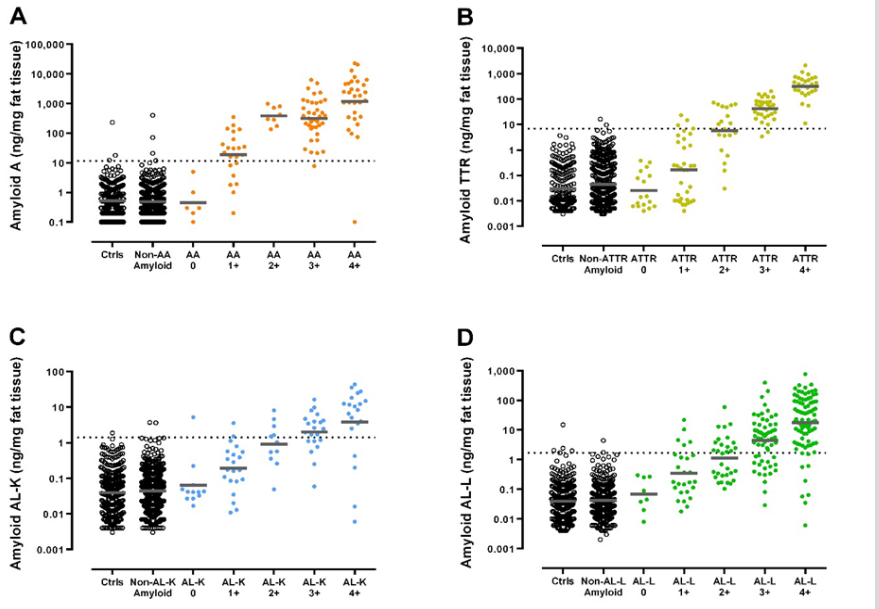

Figure 1. The ELISA-4-Amyloid results. Type (A) AA, (B) ATTR, (C) AL-K and (D) AL-L amyloid in fat tissue. In each panel all results of the respective controls and the amyloid grades of the specific amyloid type are shown. The dotted lines mark the upper reference limits and the small lines mark the means of the log-transformed values.

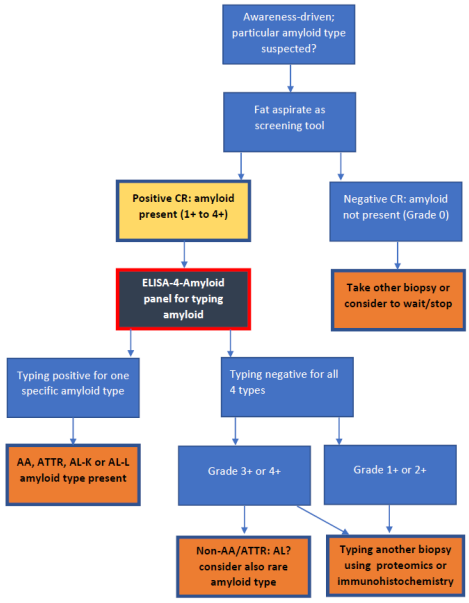

Figure 2. Decision tree of the ELISA-4-Amyloid panel for typing amyloid, starting with awareness.

CONCLUSIONS

- **Specificity of the ELISA-4-Amyloid panel is high (99%) and the sensitivity is determined by the grade of amyloid: sensitivity is high (91%) in abundant amyloid (4+), reasonable (75%) in much amyloid (3+), moderate (58%) in little amyloid (2+) and negligible (21%) in minute amyloid (1+).**
- **Immunochemical typing by ELISA of the four main characterizing proteins in fat tissue is a quick, specific and sensitive routine method for typing patients with systemic amyloidosis if ample amyloid is present.**

http://www.amyloid.nl