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TTA. Transthyretin Amyloidosis

NIHR BioResource – Rare Diseases study project

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Summary

Amyloidosis is a rare fatal disease caused by accumulation in the tissues of the body's own proteins in an abnormal form called amyloid.

After injury, infection and other diseases, debris is normally rapidly cleared from the tissues as they heal but, for reasons that are not understood, once proteins form amyloid they are removed slowly if at all. As a result, amyloid accumulates until it damages the structure and the function of the affected parts of the body, causing disease and eventually death. One of the proteins that forms amyloid, called transthyretin, particularly affects the heart, causing fatal heart failure.

Recent research in our Centre has identified, for the first time, key aspects both of the formation of amyloid by transthyretin protein and the mechanism by which such amyloid can be removed. We discovered, very surprisingly, that transthyretin amyloid formation involves the body function responsible for removal of unwanted blood clots, the so-called fibrinolysis pathway. We have also found that the clearance of amyloid from the tissues can be achieved by activation of a body function involved in defence against infection, the so-called complement system. The fibrinolysis and complement systems are both very complex, involving many different interacting proteins. There are therefore very strong grounds for believing that between individual differences in the genes controlling the two systems could importantly affect susceptibility to transthyretin amyloidosis and the extent and severity of the disease. Indeed, in a small preliminary study we have already found that most patients with transthyretin amyloidosis have one or more genes responsible for impaired complement activity, genes that are very rarely found in the general population. Other researchers have recently, independently, made related observations.

We are therefore optimistic that a large scale, thorough characterisation of the genes for the fibrinolysis and complement systems in patients with transthyretin amyloidosis may enable identification of markers for those at risk for the disease. This will be invaluable as new and effective medicines to treat transthyretin amyloidosis are just becoming available for the first time.

The NHS National Amyloidosis Centre, directly funded by NHS England, is the single national specialist referral Centre and is mandated to see all amyloidosis patients in the country. We are the largest such Centre in the world, have pioneered world leading diagnostic and evaluation procedures and have a uniquely well characterized transthyretin amyloidosis patient population.

Recruitment Criteria

Inclusion

All patients with ATTR amyloidosis and those referred to the NAC with TTR mutations who do not have clinical amyloidosis will be offered participation in this project.

Exclusion

Patients with other types of amyloid will be excluded.