PATHOGENETIC MECHANISMS AND PRECURSOR PRODUCT RELATIONSHIPS IN MURINE AMYLOIDOSIS

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ABSTRACT

Intravenous injection of $^{125}$I-labeled isolated mouse serum amyloid P component (SAP) into mice with systemic AA amyloidosis led to specific deposition of the labeled protein in amyloidotic organs. The amount correlated with the quantity of amyloid present and localized in the same distribution within the organs as the amyloid deposits. Human SAP, when injected intravenously into amyloidotic mice, also localized specifically to the amyloid deposits. These observations establish directly that circulating SAP is the precursor of the amyloid P component (AP) found associated with amyloid deposits. In addition to elucidating one aspect of the pathogenesis of amyloid deposition, these results suggest a means for selective targeting of diagnostic traces and/or effector agents to amyloid deposits in vivo.

INTRODUCTION

In all forms of localized and systemic amyloidosis with the exception of the intracerebral plaques in Alzheimer's diseases and senile dementia [1], amyloid P component (AP) is found associated with the fibrillar amyloid deposits [2, 3]. AP, a nonfibrillar glycoprotein, is found in amounts up to 15% of the mass of the amyloid deposits [4]. AP is apparently identical to a normal plasma protein, serum amyloid P components (SAP) as judged by immunochemical testing, by polyacrylamide gel electrophoresis performed either in the presence of sodium dodecyl sulfate or under non-denaturing conditions, by partial amino acid sequence analysis and by appearance in the electron microscope [2, 3]. Thus it has been assumed, although never directly demonstrated, that AP is derived from circulating SAP. It is not known however, whether SAP or AP play a role in the deposition and persistence of amyloid.