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Histotopographic evidence that amyloid deposits in sclerocalcific heart valves and other chronic lesions of the cardiovascular system are related to old thrombotic material

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Summary. Deposition of amyloid in human sclero-calcific heart valves has been reported recently as a localized age-independant and dystrophic form of amyloidosis. Histochemical studies have shown that the deposits are permanganate resistant, contain tryptophan and P component and are immunologically unrelated to any known type of amyloid fibril protein. In this study histological observations from a series of four selected sclerotic heart valves show amyloid deposition in old thrombotic material covering fusing commissures or appositional collagen on the body of the leaflets. Similar cases from extravalvular sites have been added to the series: a partly hyalinized thrombus of the left atrium, a thrombotic aneurysm of the left ventricle, 2 thrombotic atherosclerotic aneurysms of the aorta and popliteal artery respectively, and an encapsulated haematoma of the scalp. The deposits are Congo red positive with typical green dichroism in polarized light, permanganate resistant and contain tryptophan. Electron microscopy of 3 cases displays small fibrils which are typical of amyloid.

No patient showed evidence of systemic amyloidosis. The natural history of sclero-calcific valvulopathies and present observations favour the following pathogenesis: first, recurrent thrombotic deposition on thickened and fibrotic endocardium; second, degradation of a coagulation-related protein with β potential during the aging of the clot with transformation into amyloid fibrils; finally, inclusion of the amyloid in sclerotic replacement tissue.

Key words: Amyloid – Atherosclerosis – Calcification – Cardiovascular – Thrombus

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Introduction

The presence of amyloid deposits in sclero-calcific heart valves has been reported recently in human patients, as a localized and age-independent form of amyloidosis (Goffin 1980; Falk et al. 1981; Iwata 1982; Cooper 1983). The amyloid has been referred to as "dystrophic" since the deposits are observed exclusively in sclerotic and sclero-calcific lesions.

In a histochemical and immunofluorescence study, we have shown that this type of amyloid was permanganate resistant, contained the amino-acid tryptophan and that P component (AP) was associated with it (Goffin et al. 1983). The study has also shown that it was unrelated to the previously known types of amyloid fibril proteins: AA, AL, ASC_1, HPA and AE_t. It has been suggested that the deposition might be the result of chronic mechanical stress at the site of severely thickened and malformed cusps, although no clear evidence has been presented to support this assumption (Egan et al. 1982). However, further histological observations made in our laboratory show that this type of amyloid deposit is generally found in fusing commissures in the additional layers of collagen covering the surface of the original valvular tissue.

The purpose of this paper is to demonstrate that the deposits of localized "dystrophic" amyloidosis of the heart valves are associated with old thrombotic material, using histological illustrations from a series of selected cases.

Material and methods

Nine cases of localized amyloidosis of the cardiovascular system have been selected on grounds of their dystrophic environment and obvious topographic relation to thrombotic material. An additional case of dystrophic amyloid deposition has been found in an extravascular site, namely in the margin of an old encapsulated haematoma of the scalp. Age and sex of the patients, sites of the amyloid deposits and clinical diagnosis are listed in Table 1. The age of the patients ranged from 39–77 years; seven were males and three females. All samples were surgical specimens, except the mitral valve of case 2, which was removed at postmortem examination. In case 1, the patient was operated on for post-rheumatic mitral stenosis with a huge parietal thrombus in the atrium. He died shortly after the operation from acute myocardial infarction as a consequence of the embolization of amyloid-laden thrombotic material to the anterior descending coronary artery. No evidence of systemic amyloidosis was found at the autopsy of patients 1 and 2. Likewise, none of the living patients was known to have senile cardiac amyloidosis or any of the systemic forms of the disease.

In an independent series, three post-mortem clots and forty five thrombi of various ages – non organized, organized and homogenized – were screened for amyloid deposits.

All samples were fixed in 10% formalin and embedded in paraffin; 6 μm sections were stained with haematoxylin-eosin-saffron, alkaline Congo red (with alcoholic potassium hydroxide differentiation) for amyloid, orcein-Van Gieson for elastin and collagen, and phosphotungstic acid haematoxylin for fibrin.

In most cases, sections were treated with potassium permanganate prior to Congo red staining (Wright et al. 1977) and the DMAB method for tryptophan (Adams 1957). The Congo red stained sections were mounted in arabic gum-sucrose in order to prevent non-specific greenish birefringence of dense collagen bundles (Romhanyi 1971). The diagnosis of amyloid was made on basis of its selective affinity for alkaline Congo red and subsequent apple green birefringence under polarized light.

In cases n° 1–6–10, samples of formalin-fixed amyloid laden tissues were deparafinized, postfixed in 2.5% GTD and 2% OsO_4 and embedded in Epon.

Thin sections were stained with lead citrate and examined on a Philips EM 400 T.

Table 1. Clinical and histopathological data[a] in 10 cases of coagulation – related amyloid

Cases	Age (y), Sex	Site of amyloid deposition	Clinical diagnosis	Histological findings
1.	75 m	Left atrium	Large mural thrombosis chronic rheumatic endocarditis	Partly hyalinized thrombus attached to sclerotic endocardium
2.	62 f	Mitral valve	Sclerotic stenosis chronic rheumatic endocarditis	Old thrombotic deposits partly replaced by sclerotic tissue
3.	49 m	Mitral valve	Sclerotic stenosis chronic rheumatic endocarditis	Sclerotic adhesion of commissure covered by thrombotic deposits
4.	39 f	Mitral valve	Sclerotic stenosis chronic rheumatic endocarditis	Sclerotic adhesion of commissure covered by thrombotic deposits
5.	56 m	Left ventricle	Ventricular aneurism with thrombosis, resulting from myocardial infarction	Old scar of transmural myocardial infarction with partly hyalinized thrombus
6.	53 f	Aortic valve	Sclerotic stenosis chronic rheumatic endocarditis	Fibrotic infiltration of ventricularis covered by thrombotic deposits, sclerotic adhesion of the 3 commissures
7.	77 m	Abdominal aorta	Atherosclerotic aneurysm	Ulcerated calcified atheroma covered by thrombotic deposits
8.	73 m	Femoral artery	Atherosclerotic aneurysm with thrombosis	Ulcerated atheroma with micro-calcification; covered by hyalinized thrombus
9.	76 m	Popliteal artery	Atherosclerotic aneurysm with thrombosis	Ulcerated atheroma with micro-calcification, old intraparietal hemorrhage and hyalinized thrombus
10.	60 m	Scalp	Old encapsulated hematoma	Old hematoma surrounded by sclerotic tissue

[a] Exclusive of amyloid

Results

The histological features of the thrombotic or coagulation-related lesions, the precise localization of the amyloid deposits and their histochemical character are presented in Table 2. The typical macroscopic aspect of a postrheumatic sclerotic mitral stenosis with thrombotic deposition and inclusion in a fusing commissure (case n° 4) is shown in Fig. 1. Histological examina-

Table 2. Histological and histochemical aspects in 10 cases of coagulation – related amyloid

Case	Side of amyloid	Histological findings (exclusive of amyloid)	Topography of amyloid deposits	Histochemistry of amyloid	
				$KMnO_4$	Tryptophan
1.	L. atrium	Partly hyalinized thrombus attached to sclerotic endocardium	Hyalinized thrombus[a] sclerotic endocardium	R	
2.	Mitral valve	Old thrombotic deposits partly replaced by sclerotic tissue	Old thrombotic material sclerotic replacement tissue	R	+
3.	Mitral valve	Sclerotic adhesion of commissure covered by thrombotic deposits	Old thrombotic material sclerotic adhesion	R	
4.	Mitral valve	Sclerotic adhesion of commissure covered by thrombotic deposits	Old thrombotic material sclerotic adhesion	R	+
5.	L. ventricle	Old scar of transmural myocard infarction with partly hyalinized thrombus	Superficial layer of sclerotic endocardium close to hyalinized thrombus[b]	R	±
6.	Aortic valve	Fibrotic infiltration of ventricularis covered by thrombotic deposits; sclerotic adhesion of the 3 commissures	A few deposits in the old thrombotic material;[a] numerous deposits in adhesion	R	
7.	Abd. aorta	Ulcerated calcified atheroma covered by thrombotic deposits	In ulceration and close to calcifications	R	+
8.	Femoral art.	Ulcerated atheroma with microcalcifications, covered by hyalinized thrombus	In ulceration and close to calcifications		+
9.	Popliteal art.	Ulcerated atheroma with microcalcifications, old parietal hemorrhage and hyalinized thrombus	Margin of thrombus and sclerotic tissue close to ulceration;[b] margin of parietal hemorrhage	R (10% ↓)	+
10.	Scalp	Old hematoma surrounded by sclerotic tissue	Margin of bloodclot[a] in sclerosis	R (50% ↓)	?

± = weak reaction; R = resistant

[a] Fibrils in electron microscopy

[b] Presence of fibrin streaks inside the amyloid deposits

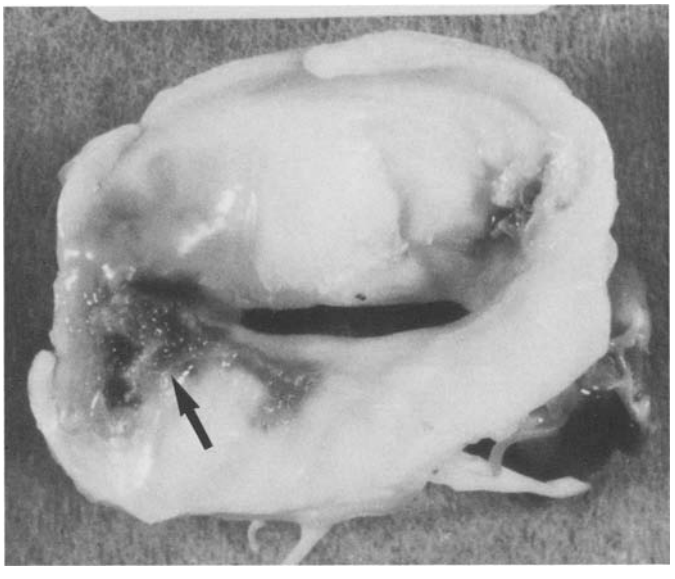


Fig. 1. Atrial aspect of a sclerotic and stenotic mitral valve in a case of chronic rheumatic endocarditis (case 4). Both commissures are fused and thrombotic material is apparent on the left side (*arrow*). The dark area of this commissure corresponds to old thrombotic material, which has been partly replaced by collagen and contain several amyloid deposits

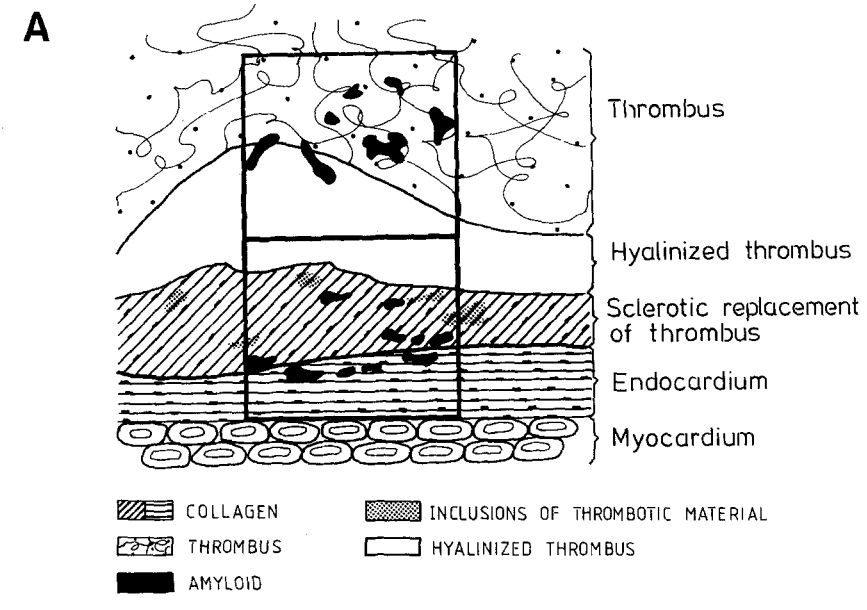
tion of the commissure revealed the presence of amyloid both in the old thrombotic material and the underlying sclerotic adhesion.

All photomicrographs are selected to demonstrate the presence of amyloid in thrombotic material (Figs. 2, 3, 5, 6) and in the area of replacement fibrosis at the margin of the thrombus (Figs. 2, 3, 4, 5) or the haematoma (Fig. 7). In the relatively superficial and hence apparently recent layers of the thrombi, amyloid forms small and more or less dense homogeneous bodies, surrounded by streaks of fibrin, aggregated platelets, leukocytes and macrophages (Figs. 2C, D, E; 4C). In older clots and in the deeper parts of layered thrombi, the amyloid is included in homogenized acellular material, which is partly replaced by collagen (Figs. 6B, C; 7). Other amyloid deposits are trapped between bundles of collagen fibers (Figs. 2F; 4B; 6C), and sometimes contain delicate streaks of fibrin.

In the atherosclerotic lesions, inclusions of amyloid are often located close to cholesterol crystals (Fig. 6C) and small calcifications.

However, no amyloid is identified in the normal tissues, whether in the heart walls, valves or arterial tunicae. Likewise amyloid is constantly absent from the walls of the small vessels.

Histochemically, the amyloid deposits are permanganate resistant and contain the aminoacid tryptophan. Resistance to permanganate is generally strong, i.e. the amyloid keeps most its initial Congophilia and green dichroism after permanganate treatment, except in the case of the old encapsulated



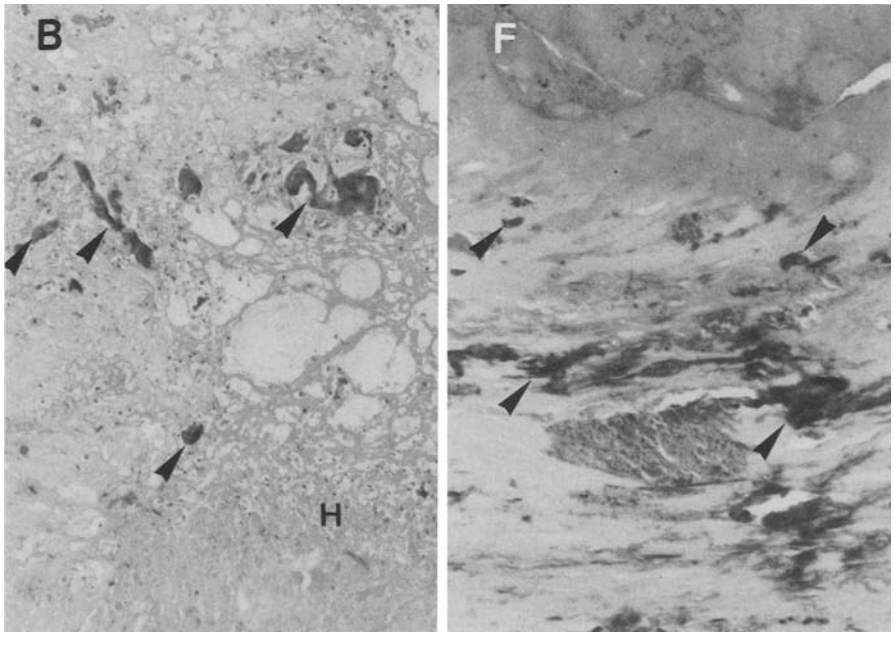


Fig. 2A–F. Schematic drawing (**A**) and set of photomicrographs **B–F** of a partly hyalinized thrombus of the left atrium in a 75 year-old male. The patient was operated upon for post rheumatic mitral stenosis (case 1). **B** Several amyloid deposits (*arrows*) in partly hyalinized (*H*) thrombus. **C**, **D** and **E** Higher magnification in ordinary and polarized light showing macrophages (*M*) and dark streaks of fibrin (*x*) in close topographical relation to the deposits; typical birefringence of Congo red stained amyloid in **D**; **F** Amyloid deposits (*arrows*) are also present in the sclerotic area covering the parietal endocardium at the base of the thrombus. (**B** Congo red × 20, **C** × **D** Congo red × 125, **F** Congo red × 50)

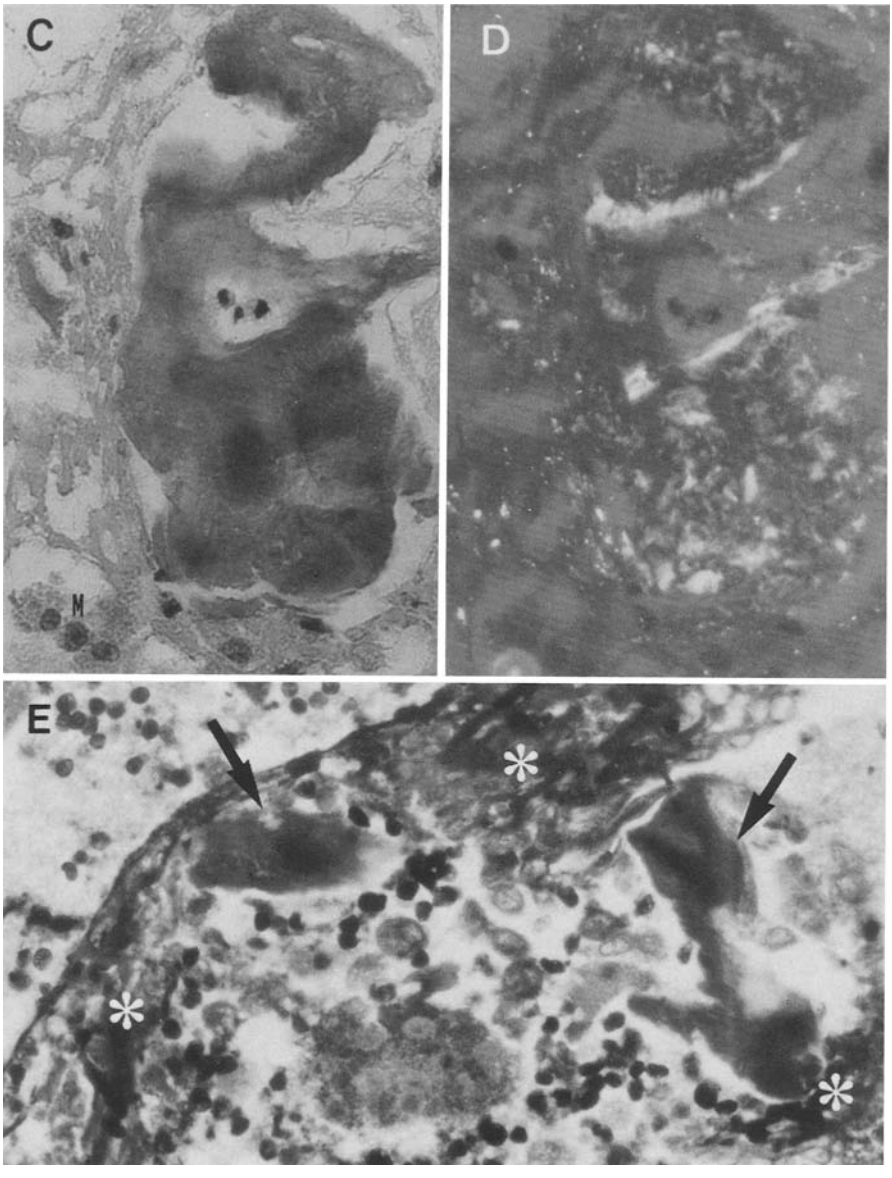


Fig. 2

haematoma (case n° 10, Table 2), where the deposits loose a great deal of their staining properties.

In the separate series of thrombi collected at random, one out of twelve homogenized clots contained Congo Red positive material with green dichroïsm. None of the other categories of thrombi nor the postmortem samples were positive.

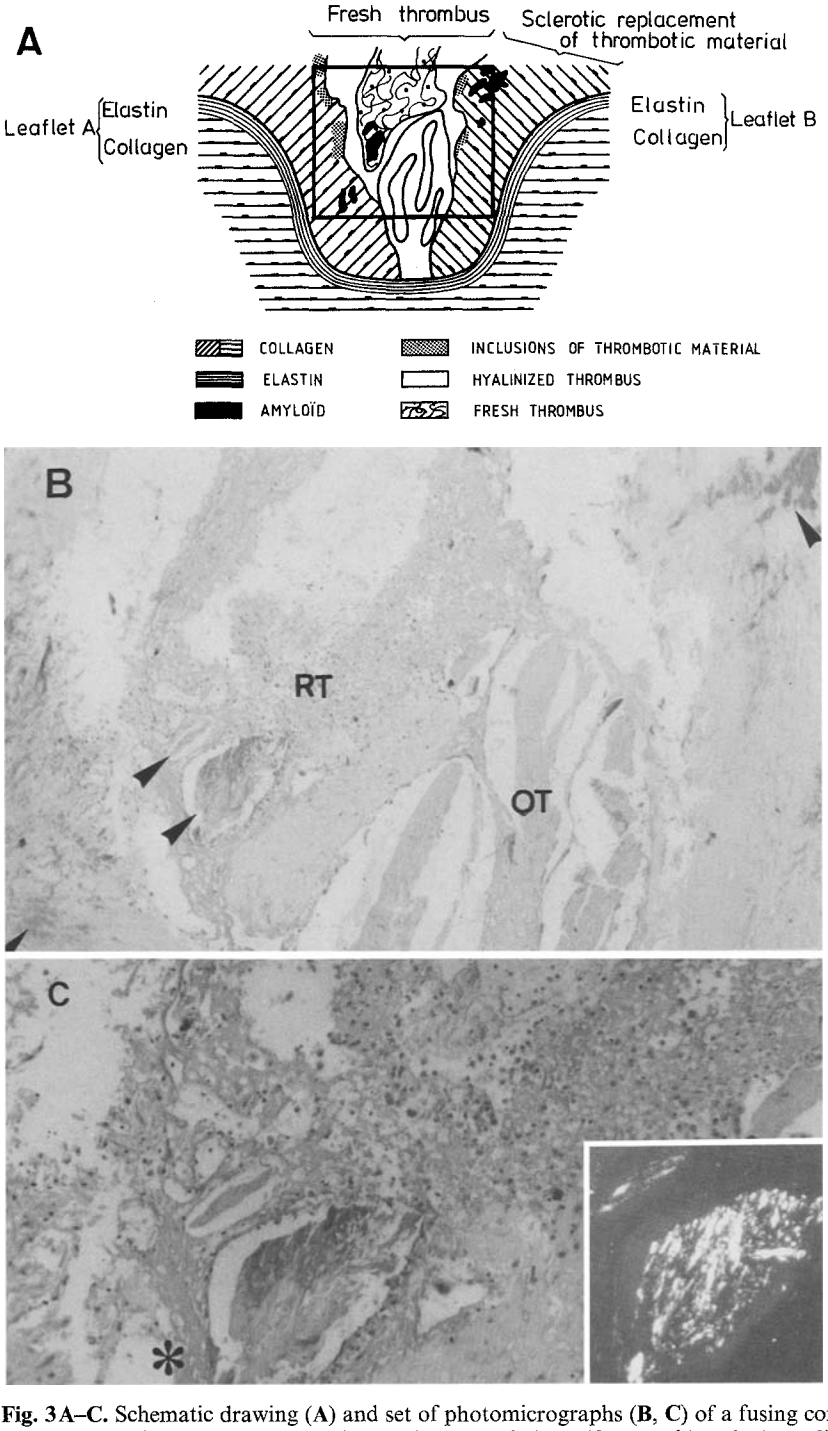


Fig. 3A–C. Schematic drawing (**A**) and set of photomicrographs (**B**, **C**) of a fusing commissure from a sclerotic post rheumatic mitral valve stenosis in a 48 year-old male (case 3): **B** Low magnification showing old (*OT*) and recent (*RT*) thrombus in the center and appositional sclerotic tissue on thickened leaflets at both sides. Congo red positive deposits (*arrows*) are seen in the thrombus and sclerotic tissue; **C** higher magnification showing fibrin streaks (*X*) and cells in the vicinity of the amyloid desposits; typical birefringence is demonstrated in *inset*. *Nota bene*: the native valvular tissue is not present in the photomicrographs. (**B** Congo red ×14, **C** Congo red ×32)

In cases n° 1, 6 and 10, extensive electron microscopic study confirmed the presence of fibrils (Fig. 8) in a background matrix of abundant fibrinous material. They showed characteristic ultrastructure of amyloid: nonbranching fibrils arranged in typical random array with a diameter of about 10 nm.

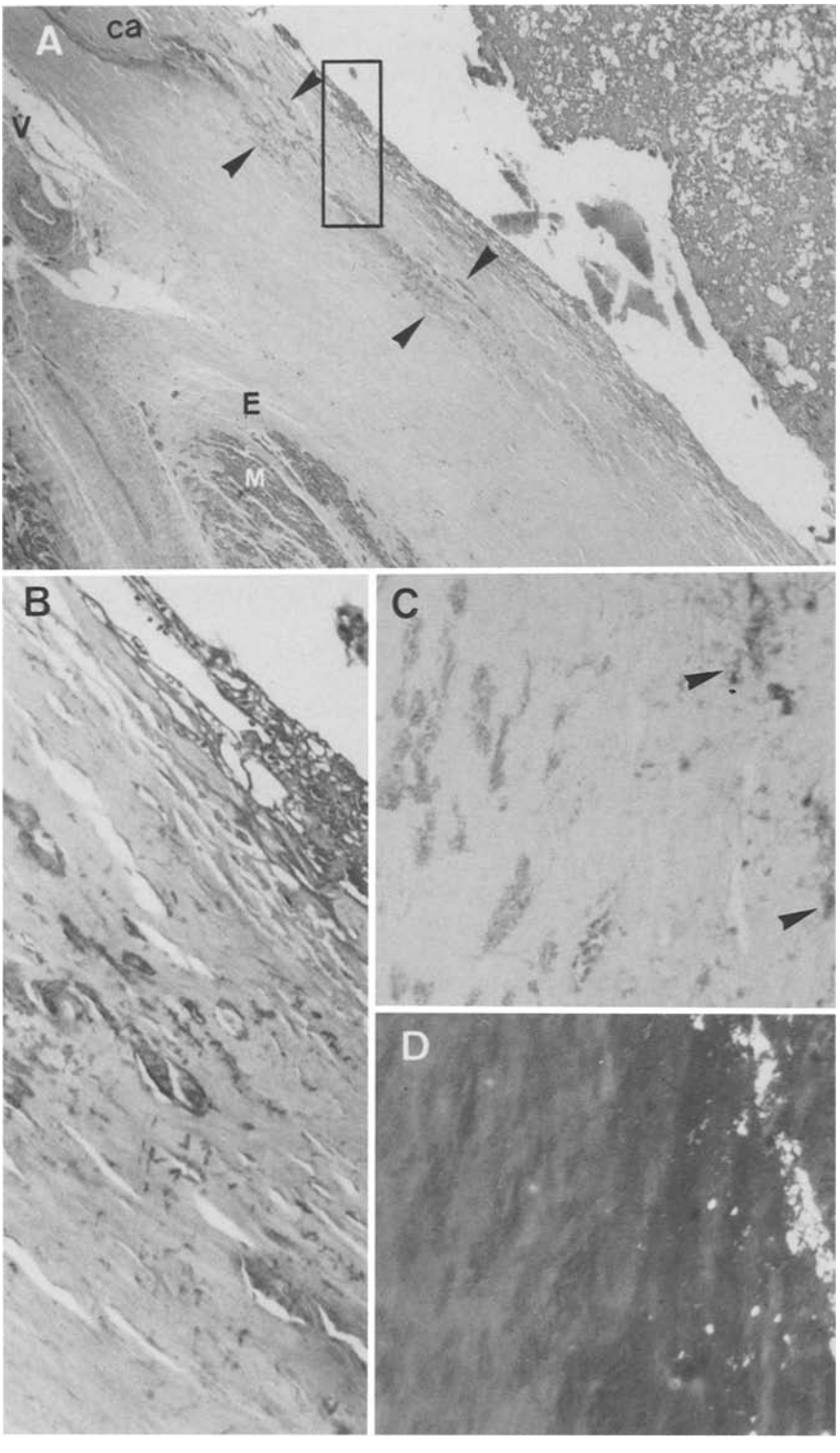
Discussion

In this selected series of sclerotic and sclero-calcific lesions associated with unresolved blood-clots, it appears that a substance which displays all features of amyloid including the typical fibrillar pattern in E.M. is deposited during the process of age-induced alterations of the clots. This is particularly obvious in synechiae of heart valve commissures and in the parietal thrombus of the left atrium (case 1), where amyloid deposits are present in proximity to and surrounded by fibrin, platelet aggregates and homogenized thrombotic material. In the other cases in the series, the old mural thrombi of post-infarction aneurysm of the left ventricle and the ulcerated atheromatous plaques of the large arteries, the amyloid deposits are mainly situated in close contact to the thrombus, exceptionally in the thrombus itself. The additional case of an old encapsulated haematoma in the aponeurosis of the skull shows that the same phenomenon can occur in long-standing extravascular clots.

All of these cases of coagulation-related amyloid deposition show some other common features: the deposits are never found in normal tissues nor in the wall of small vessels; they are permanganate resistant and contain the amino acid tryptophan. This degeneration appeared to be quite infrequent since, in our separate series of randomly collected thrombi it was detected only among old homogenized thrombi in the proportion of one out of twelve cases.

Thus our study has brought to light the hitherto unreported presence of amyloid in thrombi. Other studies, particularly immunohistochemistry, might help to determine whether the non-valvular amyloids have the same immunohistochemical characteristics as the valvular ones: a positive reaction with anti-P component and no reactivity with anti-sera to AA, ALs, ASC_1, HPA and AE_t (5). At present, both the common and the unique aspects of our series of thrombotic amyloid suggest that deposits of amyloid in sclero-calcific valves are a localized form of amyloidosis with many other potential sites of deposition in thrombotic lesions in the cardiovascular system and at the margin of encapsulated haematomata. However, the fact that amyloid deposits spare the morphologically normal parts of the cardiovascular tissues and the small vessels in the heart and in the wall of the large arteries is against the concept of a systemic form of amyloidosis, whether secondary or primary (Wright and Calkins 1981).

Central to the pathogenesis of this coagulative type of amyloidosis is the sequence of events resulting in the presence of amyloid in old thrombi. Two hypotheses can be presented: in one hypothesis, the amyloid fibrils will first appear in dystrophic sclerotic lesions; these lesions will eventually calcify, ulcerate and finally be covered with successive layers of thrombotic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material; in this hypothesis, amyloid would be detached from the bottom of the ulceration and included in the oldest layer of the thrombus. This sequence of events rules out the concept of a thrombotic origin of amyloid. The other hypothesis entails that the sequence would start with recurrent thrombotic deposition on a damaged and deformed endocardial- or intimal-surface; one particular constituent of the clot, a protein with β potential would be degraded during the aging process of the thrombus and eventually transformed into amyloid fibrils; finally, the old thrombus would calcify or be replaced by collagen, except for the amyloid which would resist to enzymatic digestion and be trapped in the heavy sclerotic appositional tissue. The second hypothesis implying a thrombotic origin for dystrophic amyloid is highly favoured by studies dealing with the natural history of chronic sclerotic heart disease in mitral and aortic stenosis (Magarey 1951; Tweedy 1956; Stein et al. 1977; Thiene et al. 1982) and valvular insufficiency (Olsen 1980). All these studies suggest that recurrent fibrin deposition with subsequent organization, scarring and eventual calcification is the major factor in the sclerotic calcific thickening of the valve. This interpretation is in accord with our everyday experience that denuded collagen and calcification in fusing commissures and on the deformed face of valves correspond to additional material which has not been covered yet by endothelial cells, rather than to ulcerated lesions (unpublished). The fact that this amyloid protein contains the aminoacid tryptophan is also in favour of its plasmatic origin, since all amyloids with a blood-borne precursor protein AA, AL, ASC_1, are tryptophan-positive. Conversely, the amyloids which are related to a local tissue precursor, the so-called APUD amyloids of the thyroid and pancreatic islets, are tryptophan-negative (Pearse et al. 1972). However, a role for the cells which constitute the walls of the vessels or of the endocardium cannot be ruled out as it has been proposed by Schlote (1965) in the case of vascular amyloidosis. If the thrombotic concept of dystrophic amyloid is correct, further investigation should aim at demonstrating that the precursor protein of this amyloid is a coagulation factor or coagulation factor-related protein with a β potential conformation and tryptophan in its amino acid sequence.

A point that deserves similar consideration is whether amyloid deposits in atheromatous lesions of the aorta (Wright et al. 1969) could be of the same type and have the same pathogenesis. In our series amyloid and pre-

Fig. 4A–D. Set of photomicrographs of the wall of a post infarction aneurysm of the left ventricle with a parietal thrombosis in a 56 year-old male (case 5). **A** Low magnification showing dense scar tissue in myocardium (*M*) and endocardium (*E*) with the thrombus in the right upper corner; the superficial layers of the sclerotic tissue correspond to replacement fibrosis of old thrombotic material and contain microdeposits of amyloid (arrows); hypertrophied vessels (*V*) are amyloid free (Ca: calcification). **B** Higher magnification of boxed area of **A**. **C** and **D** High magnification of an other area of sclerotic endocardium containing both granular non birefringent material and homogeneous deposits of amyloid (*arrows*) with typical birefringence (in **D**) (**A** haematoxylin-cosin X9; **B** haematoxylin-éosin × 50; **C** and **D** Congo red × 50)

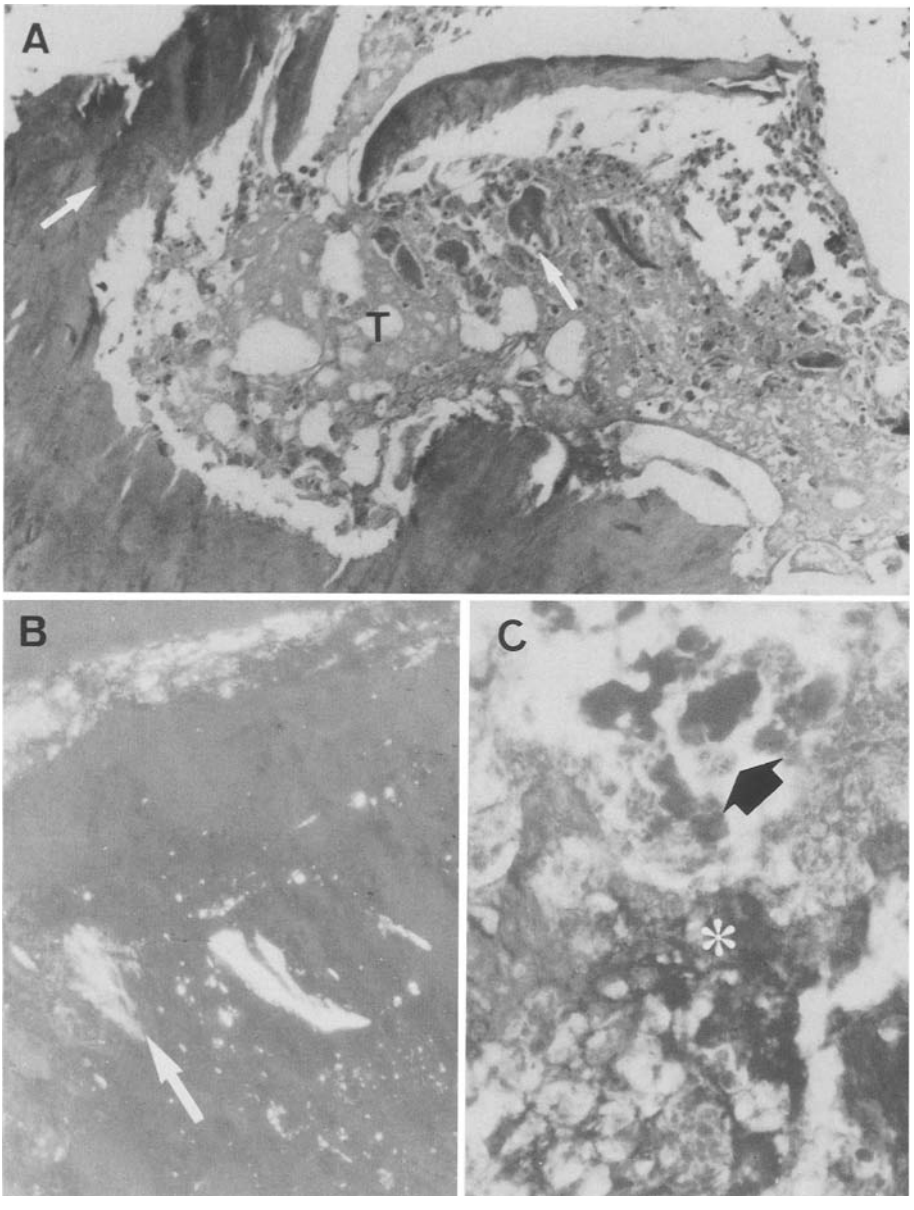

Fig. 5A–D. Set of photomicrographs of fusing commissure from a sclerotic postrheumatic aortic stenosis in a 53 year-old female (case 6). **A** Low magnification showing an area of replacement fibrosis covered by thrombotic material (*T*): amyloid deposits (*arrows*) are present both in the thrombus and sclerotic tissue; **B**, **C** and **D** high magnification of the thrombus showing macrophages and fibrin streaks (*x*) around the deposits (*arrows*). Typical birefringence of amyloid in **D**. (**A** Congo red ×12.5, **B** and **C** Congo red ×125, **D** HPTA ×125)

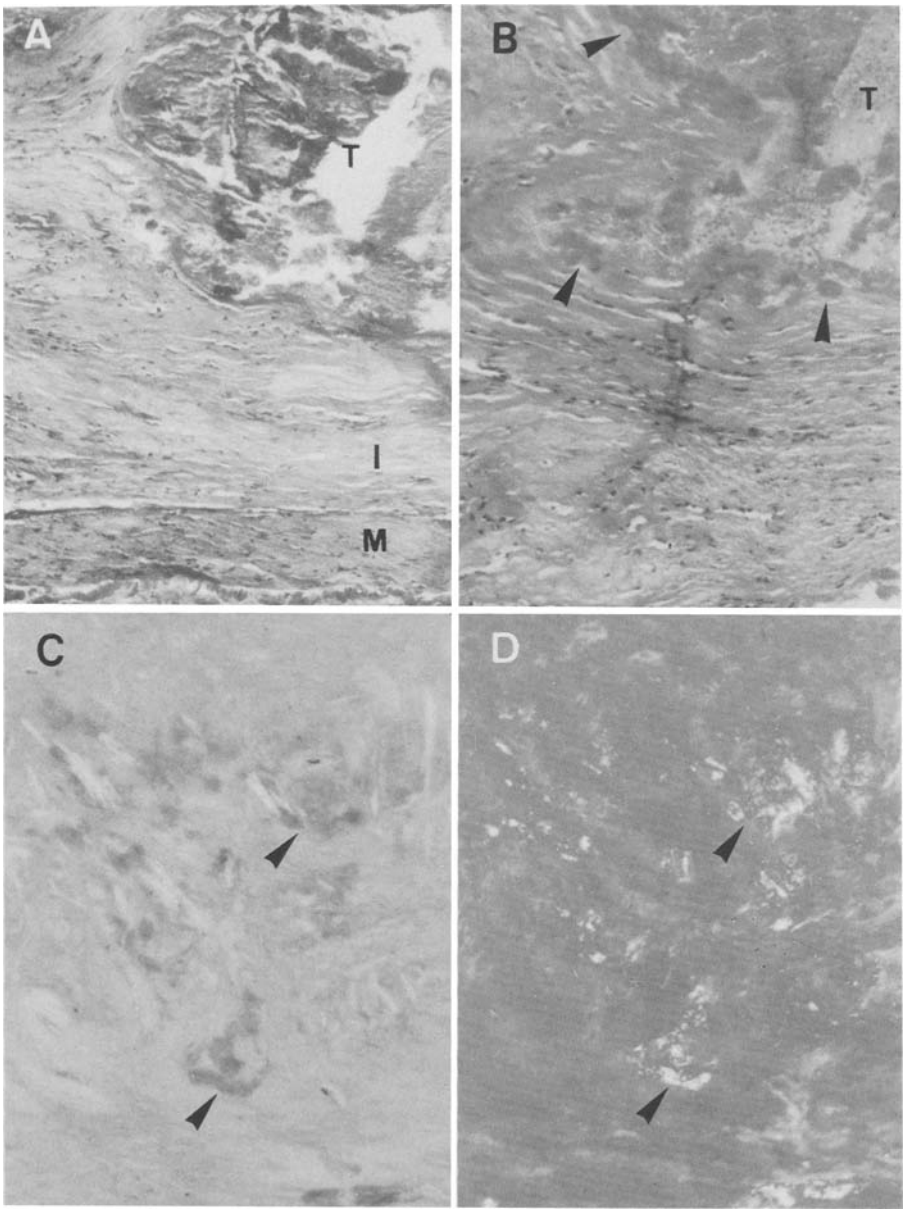

Fig. 6A–D. Set of photomicrographs of a thrombotic atherosclerotic aneurysm of the popliteal artery in a 76 year-old male (case 9). **A** low magnification showing a stretched media (*M*), a thickened sclerotic intima (*I*) and an old thrombus (*T*). **B** Congo red stain of same area with amyloid deposition (*arrows*) at the border between the old thrombotic material (*T*) and the sclerotic replacement tissue in the intima. **C** and **D** High magnification of an atheroma showing confluence of hyalinized thrombotic material, amyloid (*arrows*), dense collagen and cholesterol crystals. Typical birefringence of amyloid is seen in **D** (**A**. HE ×20, **B** Congo red ×20, **C** Congo red ×50)

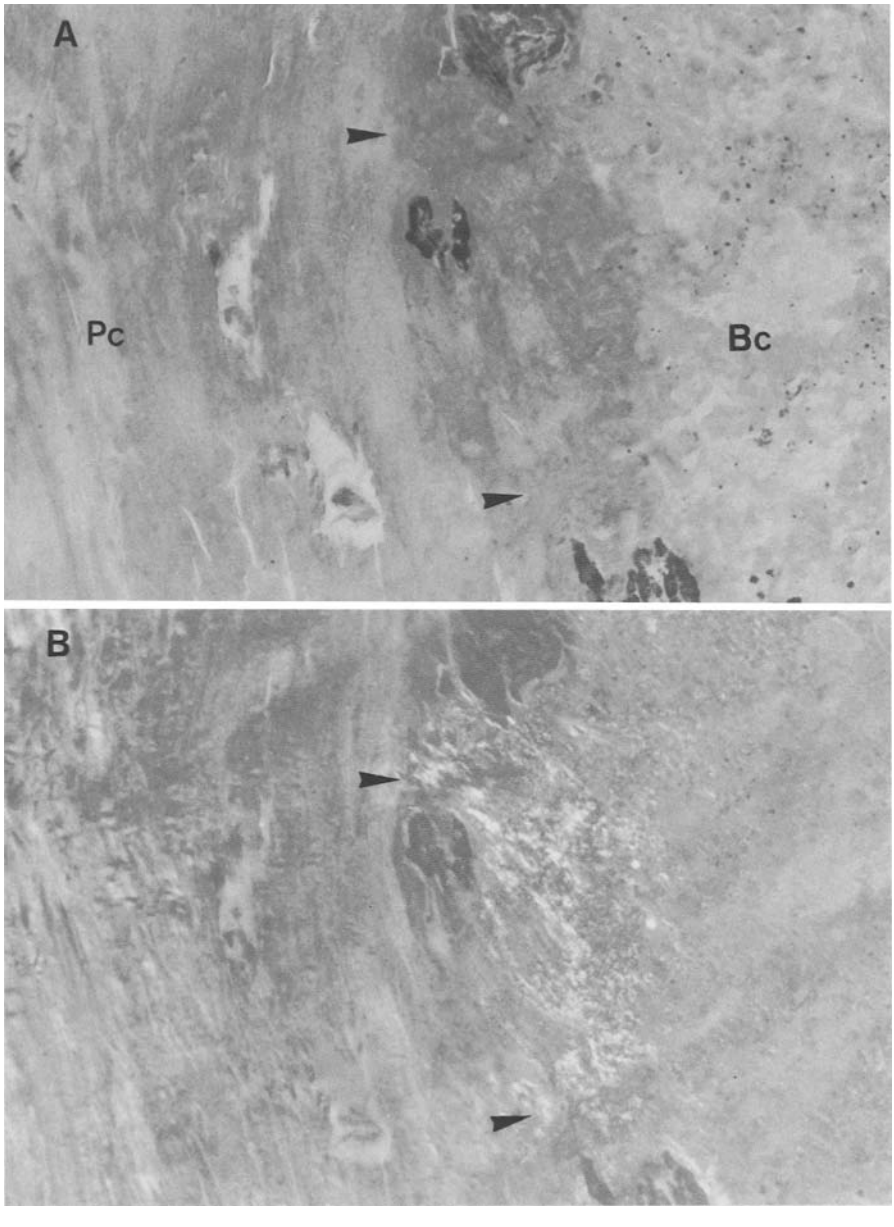

Fig. 7A–C. Photomicrographs (**A** and **B**) of an old haematoma of the scalp in a 60 year-old male (case 10), showing part of the hyalinized bloodclot (*BC*) and its thick sclerotic pseudocapsule (*Pc*): small streaks of amyloid (*arrows*) with typical birefringence (in **B**) are present in the blood clot and sclerotic tissue, together with some calcifications (*Ca*). (Congo red × 50)

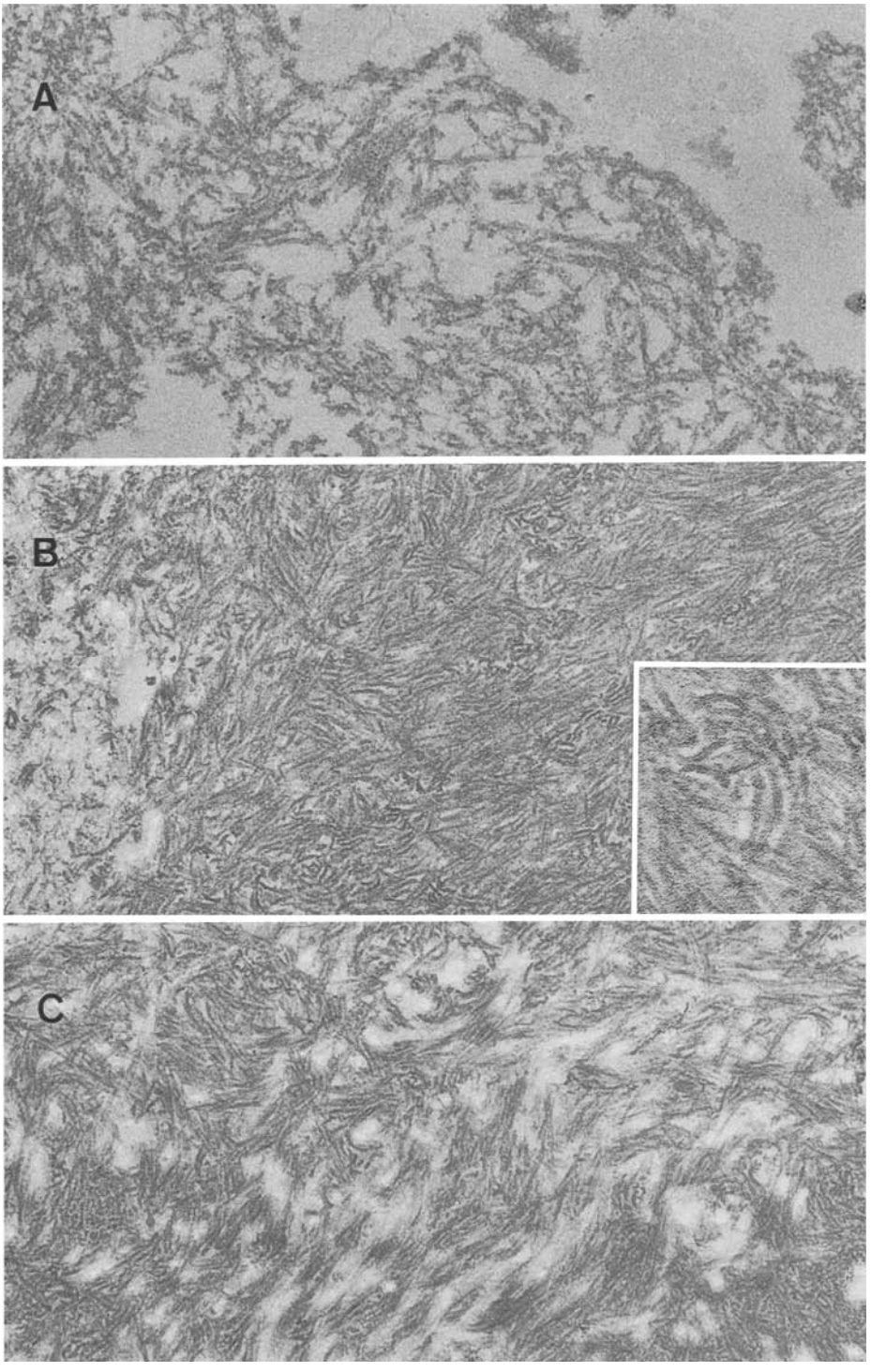

Fig. 8. Electron micrographs of straight nonbranching amyloid fibrils in cases n° 1 (**A**), 6 (**B**) and 10 (**C**). **A** Thrombus of the left atrium (× 55,000); **B** Thrombotic material of the aortic valve (× 42,500; inset: × 115,000); **C** Old haematoma of the scalp (× 42,500)

sumably a coagulation factor-related precursor protein were present in ulcerated and thrombus covered atheroma of the aorta and large muscular arteries. There might be a link between this thenomenon and Woolf's observations of a positive immunofluorescent reaction with antifibrinogen and antiplatelet antisera in mature atheromatous plaques (1981).

To conclude, this study suggests that localized so-called dystrophic amyloid of sclero-calcific heart valves is of thrombotic origin and is likely to be related to a precursor protein in the thrombus itself. The study further shows that this type of amyloid is also present in other chronic thrombotic lesions or the cardiovascular system and in old encapsulated haematomata. The deposition of amyloid fibrils and their precursor protein in ulcerated atheromas raises the question of their possible role in the continuing process of deterioration of these lesions.

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References

Adams CWM (1957) A p-dimethylaminobenzadelhyde-nitrate method for the histochemical demonstration of tryptophan and related compounds. J Clin Pathol 10:56–62

Cooper JH (1983) Localized dystrophic amyloidosis of heart valves. Hum Pathol 14:649–653

Egan MS, Goldenberg DL, Cohen AS, Segal D (1982) The association of amyloid deposits and osteoarthritis. Arthritis Rheum 25:204–208

Falk E, Ladefoged C, Christensen HE (1981) Amyloid deposits on calcified aortic valves. Acta Pathol Microbiol Immunol Scand (A) 89:23–26

Goffin YA (1980) Microscopic amyloid deposits in the heart valves: a common complication of chronic damage and scarring. J Clin Pathol 33:262–268

Goffin YA, Cornwell GG, Murdoch W, Sorenson G (1983) Microdeposits of amyloid in sclero-calcific heart valves: a histochemical and immunofluorescence study. J Clin Pathol 36:1342–1349

Iwata I, Nakamura H, Nagasawa T, Kamei T, Fujihara S, Yokota T, Uchino F (1982) Small deposits of amyloid in surgically removed heart valves. Acta Pathol Jpn 32:23–29

Magarey FR (1951) Pathogenesis of mitral stenosis. Br Med J 1:856–857

Olsen ECG (1980) The pathology of the heart, 2nd edition. The Macmillan Press Ltd, London

Pearse AGE, Ewen SWB, Polak JM (1972) The genesis of APUD amyloid in endocrine polypeptide tumors. Histochemical distinction from immunamyloid. Virchows Arch (Cell Pathol) 10:93–107

Romhanyi G (1971) Selective differenciation between amyloid and connective tissue structures based on the collagen specific topo-optical staining reaction with Congo red. Virchows Arch (A) 354:209–222

Schlote W (1965) Polarisationsoptische und elektronen mikroskopische Beobachtungen bei „Drusiger" Degeneration der Hirnrindengefäße im Senium. Proc V internat Congr Neuropath, Zürich 1965

Stein PD, Sabbah HN, Pitha JV (1977) Continuing disease process of calcific aortic stenosis. Role of microthrombi and turbulent flow. Am J Cardiol 39:159–163

Thiene G, Bortolotti U, Scarin V, Valfrè D, D'Este R, Talenti E, Valente M, Pennelli Natale (1982) Chronic rheumatic mitral disease: pathological study on 73 surgical explants. Pathologica 74:99–110

Tweedy PS (1956) The pathogenesis of valvular deformity in rheumatic heart disease. Br Heart J 18:173–185
Woolfe N (1981) Thrombosis and atherosclerosis. In: Bloom AL, Thomas DP (eds), Haemostasis and thrombosis. Churchill Livingstone, Edinburgh, pp 527–553
Wright JR, Calkins E, Breen WJ, Stolte G, Schultz RT (1969) Relation of amyloid to aging. Medicine 48:39–60
Wright JR, Calkins E, Himphrey RL (1977) Potassium permanganate reaction in amyloidosis. A histological method to assist in differentiating forms of this disease. Lab Invest 36:274–281
Wright JR, Calkins E (1981) Clinical – Pathologic differenciation of common amyloid syndromes. Medicine 60:429–448

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Note added in proof

In a subsequent study, an additional case of amyloid-related thrombosis was found in the parietal thrombus and sclerotic scar of a left ventricular aneurism in a 55 year old male. The presence of amyloid fibrils in the thrombus was confirmed by transmission electron microscopy.