Characteristic Association of Congenital Arterio-Venous Fistulas and Segmentary Arterial Fibrodysplasia: Monomelic Angiodysplastic Syndrome

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Abstract

The clinical, arteriographic and histological study of 5 cases of monomelic congenital arterio-venous fistulas proposes some findings about their pathogenetic thesis.

The association of arterial fibroplasia and congenital arterio-venous fistula is seen as caused by hemodynamic alteration and particularly by the embryogenetic changes which occur simultaneously.

These observations suggest the presence of a syndrome with characteristic monomelic anomalies.

Introduction

Although their number is limited, descriptions of arterial aneurysms of the upper and lower limb, associated with congenital arterio-venous fistula, can be found in the literature.[2,3,12,4] These are generally concerned with one limb only (are monomelic) and have a topographic disposition and a characteristically repetitive clinical manifestation.

In the histological study of these cases, structural modifications of the normal wall components in the arteries upstream of the arterio-venous fistula were noted. As is typical of these pathologies, these modifications principally take the form of a fragmentation or complete absence of the internal elastic lamina and a noteworthy elastotic fibrodysplasia of the media.

Allowing that hyperdynamic factors alone cannot be the cause of these profound histopath-

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ological changes — which are never found in acquired arterio-venous fistulas, whether they are traumatic or arterio-venous fistulas for hemodialysis[13] — consideration is given to the moment of vascular embryogenesis as the possible pathogenetic cause.

With these points in mind, together with the findings of our study of several cases delineated below, we can attempt to give a systematic collation to this particular angiodysplastic syndrome.

Materials & Methods

With the intention of finding a pathogenetic justification for the appearance of these modifications of the arterial wall, and their possible connection to the presence of congenital arterio-venous fistulas, we studied, from a clinical and morphological viewpoint, a number of cases demonstrating this characteristic appearance. The methods employed were directed toward the discovery, not only of the presence of arterio-venous shunts, but of the hemodynamic problem in the vessel network of the affected limb, along with the concomitant lesions of the various tissues above and below the fistulas.

Case Reports

1) O.B. — a man of 46, since birth a carrier of arterio-venous fistulas in the upper right limb, with cutaneous nevi on the arm and shoulder which became evident a few months after birth with the appearance of numerous ectatic and tortuous superficial veins. At the age of 30, a symptomatology determined by relative ischemia in the area downstream of the arterio-venous fistula appeared, obliging the patient to undergo 3 amputations of fingers of the right hand. Numerous arterio-venous fistulas were shown.

Angiographically examined, they resulted localized for the most part in the forearm, with a humeral artery aneurysm at the elbow and a dilated and tortuous aspect of both the proximal humeral and axillary and subclavian artery (Figure 1 a,b,c) (Figure 2 a,b) (Figure 3 a,b).

2) O.F. - a man of 44, from birth a carrier of arterio-venous fistulas in the left forearm which became evident at about the age of 12 with the appearance of considerable venous ectasias, especially in the cephalic vein. In recent years, this pathological finding had grown progressively worse, trophic ulcers having developed on the fingers of the ipsilateral hand. Angiographic examination demonstrated a large number of arterio-venous fistulas at the proximal and distal thirds of the forearm, principally at the derivation of the radial artery, associated with a large aneurysm of the humeral artery at the elbow, together with a dilated and tortuous aspect of the radial, ulnar and interosseus arteries (Figure 4 a,b,c,d).

3) M.P. — a girl of 15 and a carrier since birth of arterio-venous fistulas in the upper left limb which became evident at about 12 years of age with the appearance of a pulsatile swelling at the middle third of the arm. The limb had been slightly larger in size than the right limb since infancy. Angiographically, we observed a great tangle of arterio-venous fistulas at the proximal third of the forearm, along with a large spindle-shaped aneurysm in the middle and lower third of the humeral artery (Figure 5 a,b,c,d,e).

4) C.D.P. — 26 years of age. Arterio-venous fistulas present since birth in the left foot, clinically demonstrated by hyperthermia, distension of the veins of the limb and a thrill at the

internal malleolus. Angiographically, we identified a considerable tangle of arterio-venous fistulas in the foot and a small aneurysm at the end of the posterior tibial artery, as well as uniform dilatation of the three main arterial vessels of the leg (Figure 6 a,b,c) (Figure 7 a,b,c).

5) A.B. — a woman of 26, microcythemic, since birth a carrier of arterio-venous fistulas, clinically demonstrated by the hypertrophy of both the soft and bony tissues and ectatic venous formations of the dorsal side of the fore-foot. The condition had been aggravated in recent years by the appearance of trophic ulcers on the foot, thereafter improving and recurring. Angiographically, the presence of numerous arterio-venous fistulas in the foot was noted, along with an aneurysm in the most distal part of the posterior tibial artery.

Hemodynamic Studies

In all the cases considered, *hemogasanalysis* showed marked variations in the gas analytical parameters between the affected limb and its ipsilateral. These were represented by an arterialization of the blood in the large venous collectors upstream of the shunts and a significant desaturation quota in the parts more peripheral to the arterio-venous fistulas.

Peripheral venous pressure taken directly in the cephalic vein of the arm or in the saphenous vein of the leg, proximal to the shunts, was 2 to 4 times greater than that of the controla-

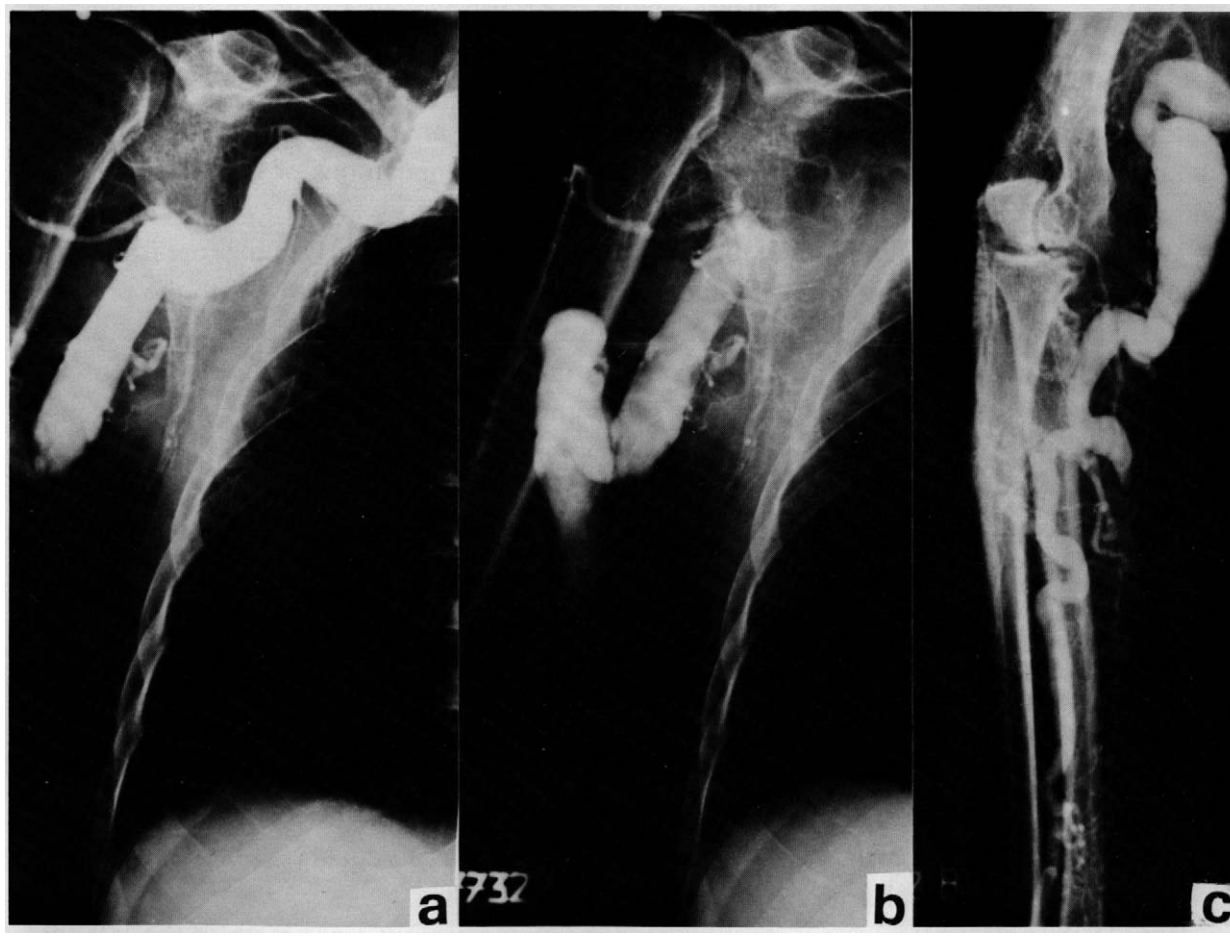

FIG. 1A,B,C. (A,B) Megadolichoartery aspect of both the subclavian and axillary. (C) Humeral artery aneurism at the elbow.

teral limb, thus demonstrating venous hypertension, even in those cases where no great varicosities were objectively evident.

Photoplethysmography tended to show a net reduction of the sphygmic wave in all the fingers of the limbs affected — an expression of a decrease in the flow volume determined by the theft that takes place at the level of the arterio-venous shunts. A wave morphology, unchanged in all its components, also appeared, as was expected, due to the normal constitution of the peripheral vessels on which the examination was carried out.[15]

The Doppler Study performed in various sectors[12] showed a high basic flow in the arteries afferent to the shunts. This pulsatility was maintained, never falling below the zero line, as was a slowing down of the rising and falling phases of the wave, due to a diminution of the peripheral resistances and the changes that develop in the arterial wall. A decomposition of the descending part of the wave also shown. The recording demonstrated a multi-directional,

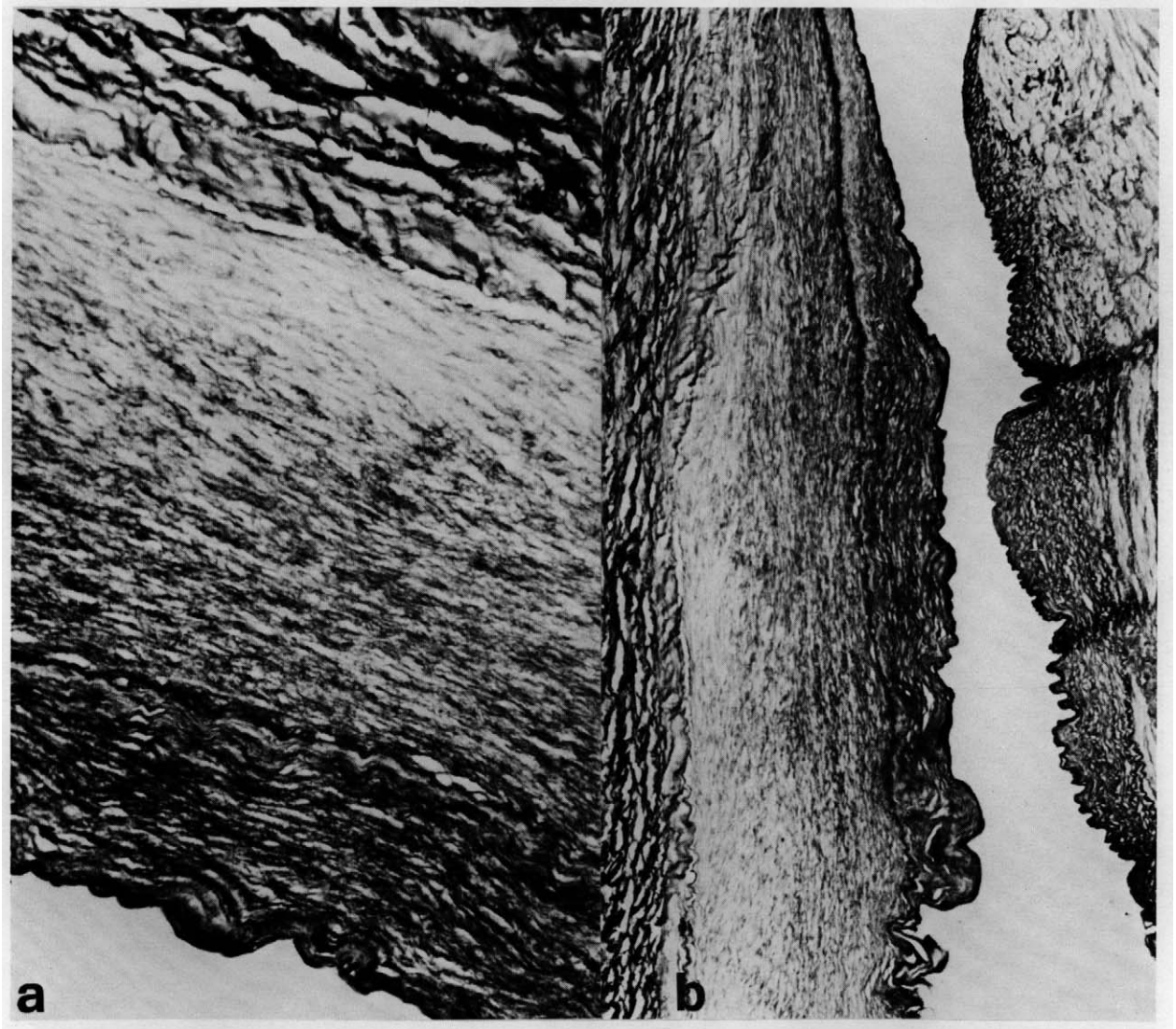

FIG. 2A&B. (A) Artery wall: Wide-spread fibrosis of intima, media and adventitia (Weigert × 60). (B) With more enlargement internal elastic lamina shows itself delaminated, while in the media elastic fibres increase and external elastic lamina disappears (Weigert × 160).

tumultuous flow in the fistulous areas. In the efferent veins, it showed a marked increase in wave pulsatility and an increase in total flow — an indication of arterialization of the vein.[12]

Histological Studies

The histological study, systematically carried out in all the cases observed, made it possible to show changes in the fistulous areas, at both artery and vein level.

Artery:

From studies made by various authors of the course taken by acquired arterio-venous fistula[6,8] we know that the hemodynamic disturbance caused by arterio-venous fistula is responsible for the well-defined alterations in the arterial wall. The artery maintains its normal organization. It loses its elastic muscular component however. This appears markedly diminished and replaced by extensive fibrosis. In other case[12,13] fibromuscular hyperplasia was observed. Usually, the internal elastic layer is preserved. Diffuse calcifications can be observed,

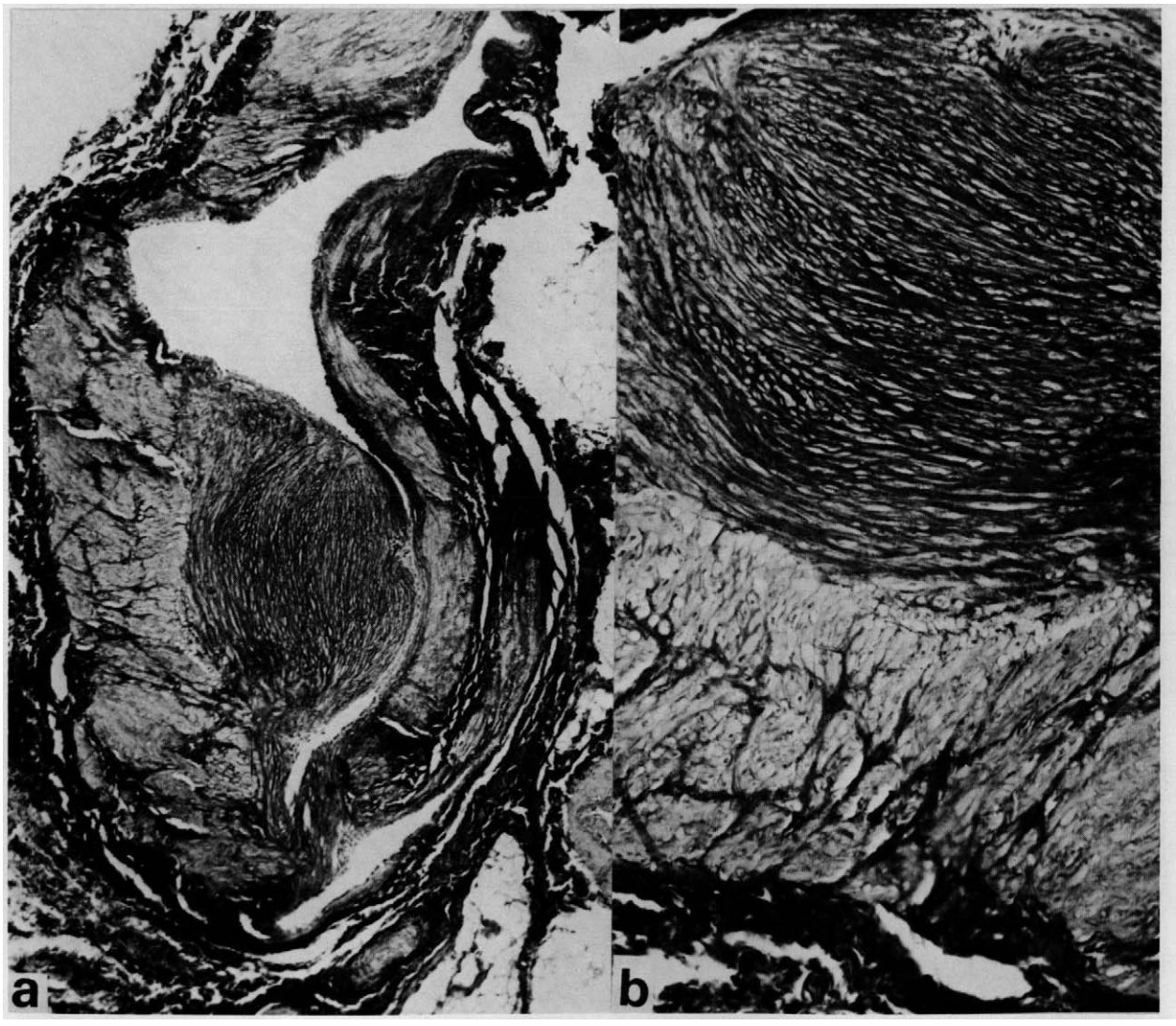

FIG. 3A&B. (A) Vein wall with wide-spread intimal thickening. Media shows unequal thickness and fibrotic areas (Van Gieson with elastic tissue stain × 60). (B) Larger picture detail of the intimal thickening. (Van Gieson with elastic tissue stain × 160).

as can precocious arteriosclerotic deposits. In the arteries upstream of the congenital arterio-venous fistula, the changes are notably different.

Intima:

There are diffuse fibrotic patches with rounded aspects in which numerous elastic fibres are found (Figure 4 c,d). The internal elastic lamina appears fragmented, interrupted, or completely absent. In some areas, the delaminations bring about a proliferation towards the media.

Media:

The media appears thinned out at points, at others, thickened. Above all, it is diffusely disordered. The muscle fibres disappear and are replaced by fibrosis and elastic proliferation (Figure 2 a,b). Such an aspect is visible up to the adventitia, which is not clearly distinguishable from the other components of the vessel wall.

These elastic fibres are separated by dense collagen tissues in which few smooth muscle cells are found. The elastic fibres appears to develop within the area of fibrosis, at times with aspects of proliferation, at others, of degeneration. This finding, defined as non-inflammatory evolutive arterial dystrophy[3] does not seem to quite fit the arterial dysplasia classification.

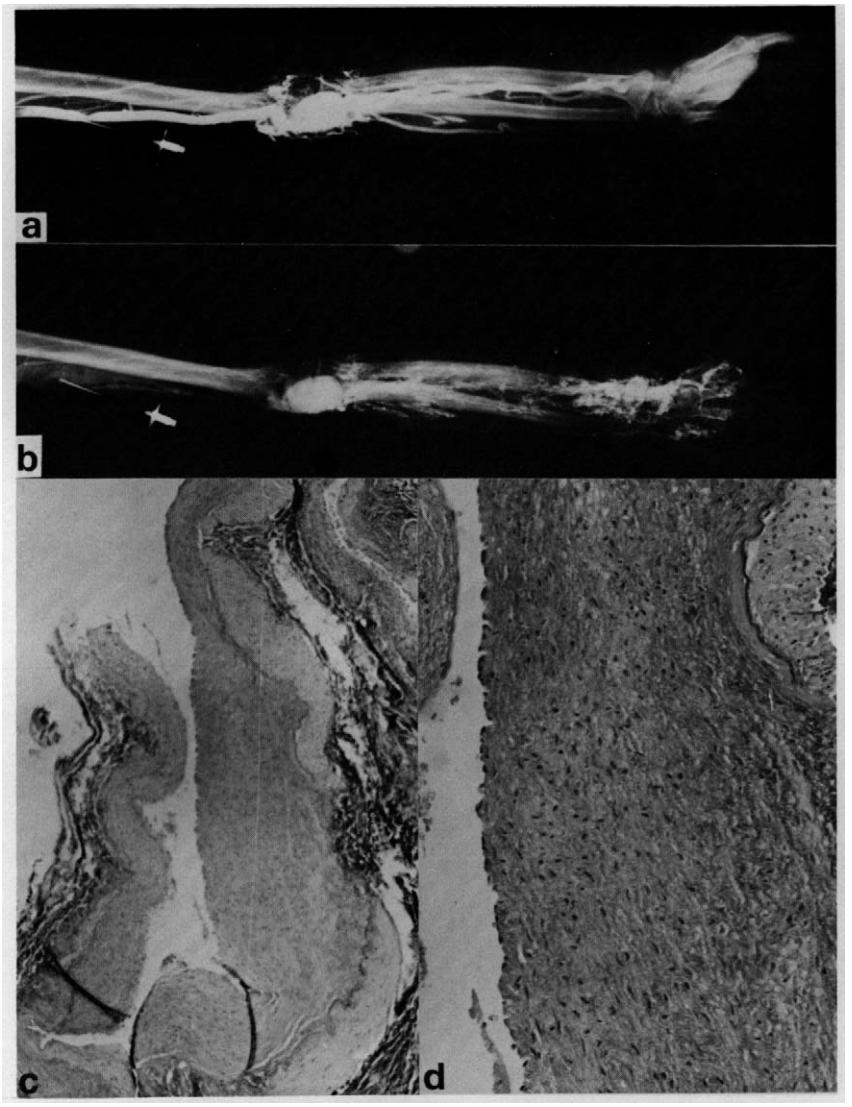

FIG. 4A,B,C&D. (A) Aneurysm of the humeral artery of the elbow. (B) Large number of arterio-venous fistulas mainly at the third distal of the forearm. (C) Diffusely thickened intima and interrupted internal elastic lamina of artery wall. Media itself is directly joined with intima, note remarkable sclerotic adventitia. (Van Gieson with elastic tissue stain × 60). (D) Artery wall detail with internal elastic lamina interruptions and elastic fibres again bare. Note remarkable intimal thickening (Van Gieson with elastic tissue stain × 160).

Adventitia:

This appears normal in nearly all sections observed — even if partly affected by the fibrosis of the media.

Vein:

The veins appear affected by serious sclerofibrotic reactions of the media and adventitia, and with considerable fibromuscular hyperplasia of the intima (Figure 3 a,b).

Discussion

Congenital arterio-venous fistula is one of the parts of the vast chapter of angiodysplasias where classification is still an object of great controversy.

The morpho-anatomic aspect of congenital arterio-venous fistula depends principally on the stage of vascular embryogenesis in which a change in development takes place. Arterio-venous angiodysplasia appears to be the result of arrested maturation at the reticular or trunk stage. Such an arrest at the plexiform stage brings about an angioma.[1] Thus, in agreement with

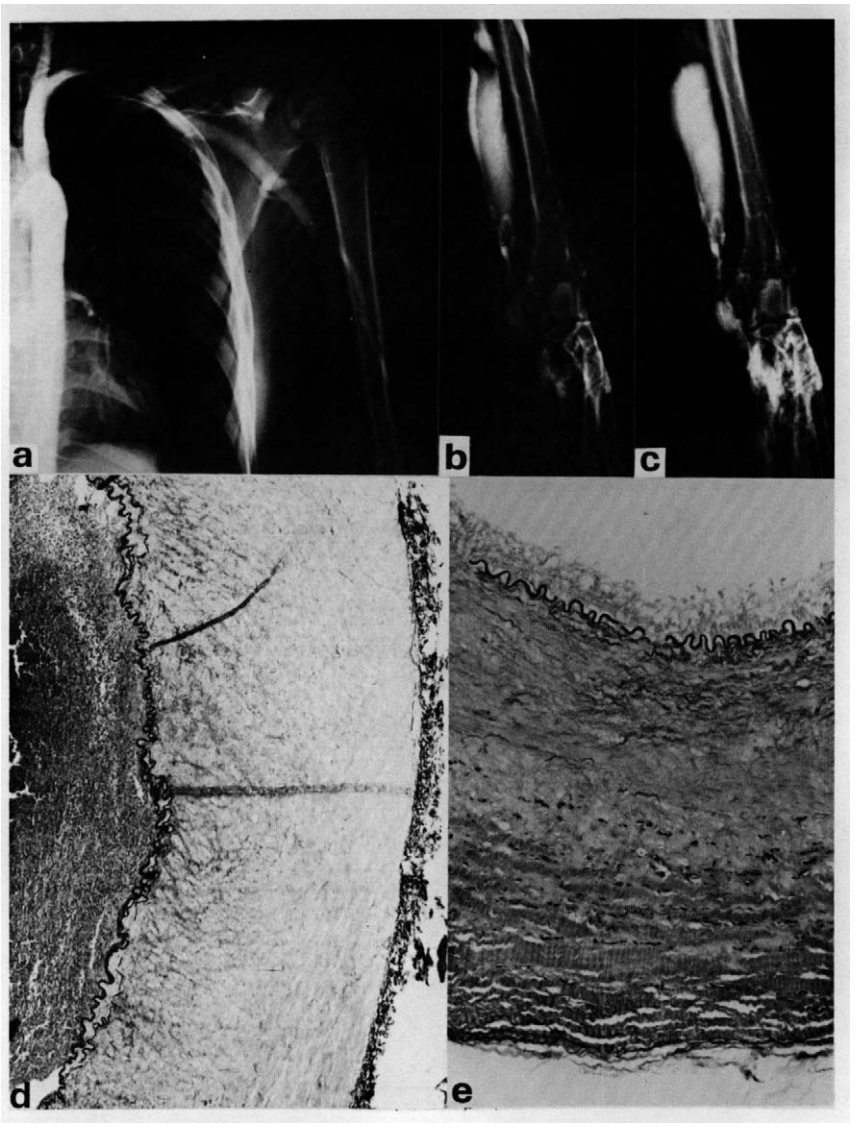

FIG. 5A,B,C&D. (A) Axillary artery selective arteriography. (B) Omeral aneurysm and arterio-venous fistulas at the proximal third of the forearm. (C) Diffuse internal elastic lamina delaminations with note thickened media in the artery wall (Van Gieson with elastic tissue stain × 60). (D) Artery wall detail with internal elastic lamina interruptions and thickened media, where are fragmented muscular fibres and neoformed elastic fibres (Van Gieson with elastic tissue stain × 160).

Malan and Puglionisi,[7] we may define congenital arterio-venous fistulas as either trunk or reticulated in origin.

From an anatomo-clinical viewpoint, arterio-venous angiodysplasias may be classified into three groups: regional forms; localized forms, and systematic forms.[8] The regional forms (those considered herein) are the most common and for the most part affect the limbs where hyperdynamic trunk arterio-venous fistulas generally appear. The hemodynamic imbalance that takes place in the main arterial and venous collectors proximal to the shunts causes structural defects in the vessel walls. These, in turn, are responsible for the appearance of dilated and tortuous artery and varicose venous changes.

As is usual, in the case we considered this phenomenon is observed in the arterial wall of proper aneurysms without there being any apparent secondary pathogenetic cause. In fact, in

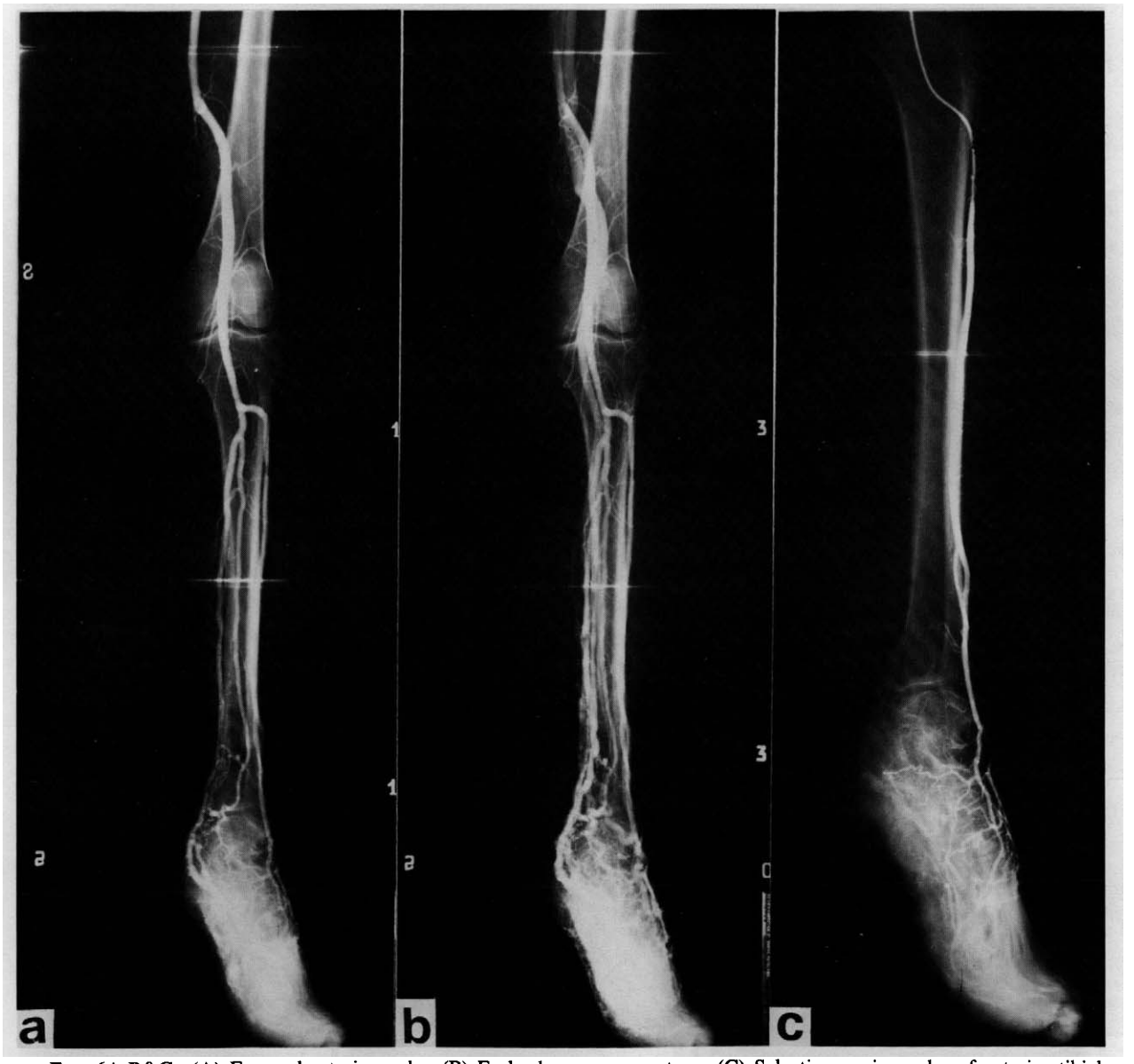

FIG. 6A,B&C. (A) Femoral arteriography. (B) Early deep venous return. (C) Selective angiography of anterior tibial artery.

acquired arterio-venous fistulas, in which only the hemodynamic factor is of any importance, real aneurysms are never found — or only after a considerable period of time (say, 5 years) has elapsed from its beginnings.[6] The histological study carred out on the wall of these congenital aneurysms revealed some particular changes: principally a fragmentation or complete absence of internal elastic lamina and a fibroelastosic dysplasia of the media.[2,11,14]

Such lesions are never found in acquired arterio-venous fistulas where the internal elastic lamina is always well represented along its entire extension. The media, however, appears to be the normal reaction to the hyperdynamic stimulous. This, then, sets in motion a process of malnutrition and, therefore, progressive degeneration of the vessel — most likely due to the increase in flow speed and stretching of the vessel wall and to the partial occlusion of the vasa vasorum.[9] The hypoxia of the arterial wall is responsible for important modifications in the smooth muscle cell.[10]

The genesis of the relative elastic proliferation remains difficult to account for. However, there are several hypotheses which seem more feasible than others:

1) A congenital reduction of the muscle component might be a concomitant factor in arterio-venous fistula. This would bring about a reduction in the resistance-consistency of the

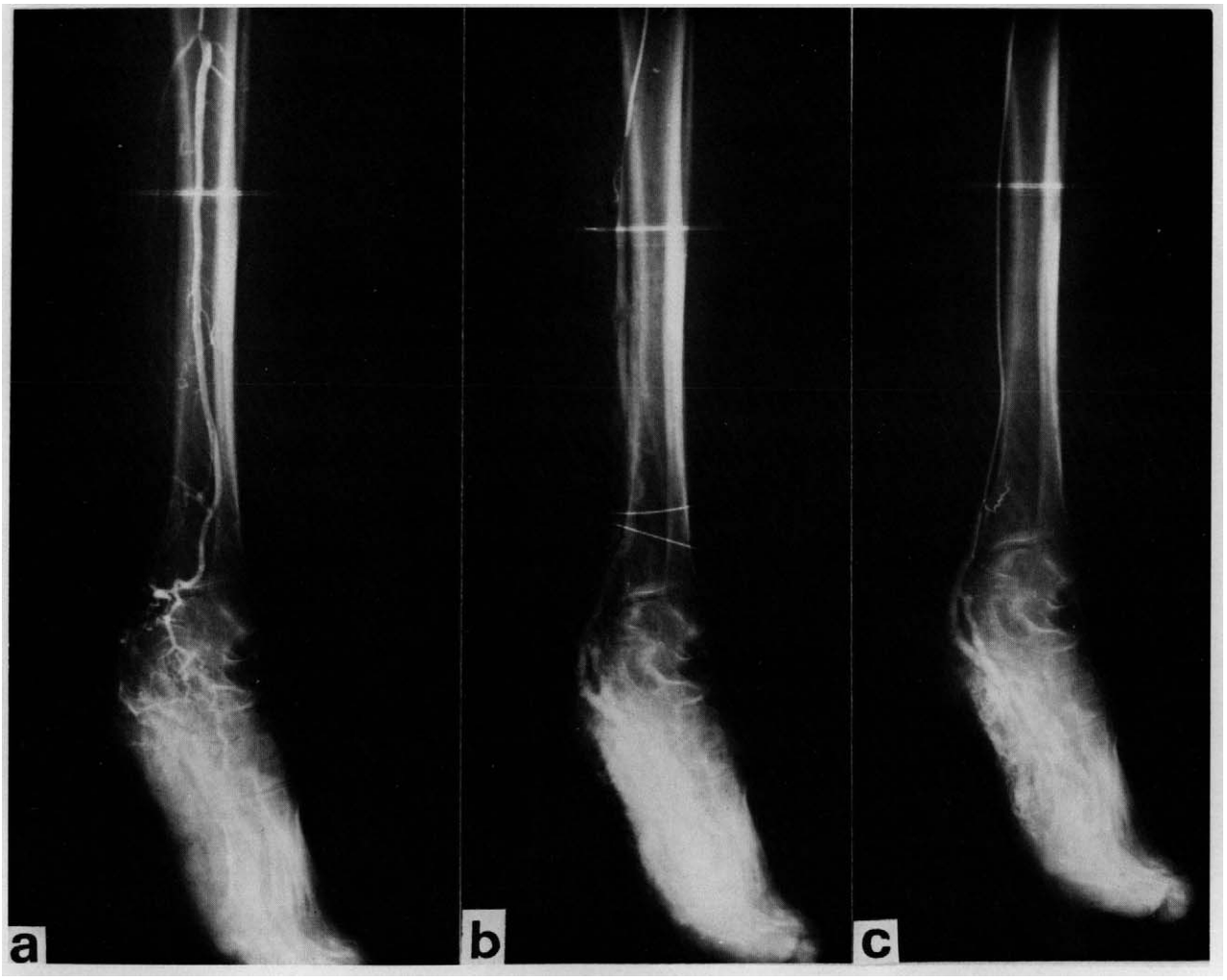

FIG. 7A,B&C. (A) Selective angiography of peroneal artery. (B,C) Selective angiography of posterior tibial artery.

wall. Then, under hyperdynamic stimulous, breakage of the internal elastic lamina as well as the other elastic structures would result — breakage which the primitive cell (smooth muscle cell) then attempts to rectify by means of a subsequent reparative fibroelastic proliferation.

2) Under increased pressure, a congenital alteration of the internal elastic lamina could cause, besides the usual fibrotic response, a complete reversal of the pluripotentiality of the smooth muscle cell to produce elastin.

3) An altered development in the post-natal life of various wall structures could occur. In fact, considering the vascular apparatus of an organism from birth to its full development, we can see how smooth muscle cells take on a fundamental role in both lengthways and widthways vessel growth — and in particular of those of the internal elastic lamina, where they continue to produce elastin. Certainly, a stimulous like the hyperdynamic one in arterio-venous fistula, present from birth, would be sufficient cause of altered internal elastic lamina, bringing about the above-mentioned changes along with the appearance of those sclero-fibro-elastotic phenomena inherent in congenital arterio-venous fistula.

Therefore, it is reasonable to consider the appearance of these aneuryms the result of a congenital defect of the arterial wall subsequently brought out by the hyperdynamic stimulous caused by arterio-venous fistula.

This would appear to be confirmed by the consideration of the so-called trunk evolutive stage of the vascular embryogenetic process in which we can observe:

1) the topographic differentiation of the arteries and veins due to coalescence of the capillaries;

2) the histological differentiation of the arteries and veins due to the incorporation of mesenchymal material.

Pathological change would, therefore, be the cause of such anomalies as:

1) trunk arterio-venous fistula, arterial and venous angiomas;

2) dysplastic or mesenchymal arterial aneurysms.

It is clear how the anomalies — congenital arterio-venous fistula and segmentary arterial fibrodysplasia — though appearing at the same embryogenetic stage, clinically manifest themselves as though one were the consequence of the other and not an expression, diverse though concomitant, of the same angiodysplastic syndrome. This last is clinically characterized by a repetitive evolution starting with these hyperdynamic arterio-venous fistulas. The initial appearance of marked distension of the veins, hyperthermia, progressive macrosomia of the affected limb and, at times, of the simultaneous presence of capillary angiomas linked to disequilibriums of the plexiform stage (never in the form of proper metameric distribution cutaneous nevi, as in the Klippel-Trenaunay Parkes-Weber syndrome, however) is subsequently followed by the formation of aneurysmatic ectases and the appearance of peripheral trophic lesions caused by the distal hypoperfusion relative to the arterio-venous shunts steal syndrome.

A single origin for this syndrome thus appears reasonable. An awareness of the presence of congenital lesions in the arterial wall, together with the persistance of congenital arterio-venous fistula, can also explain the unsuccessful surgical therapy of these lesions.

Concluding, therefore, we maintain that the aneurysm and congenital arterio-venous fistula

are part of a single angiodysplastic syndrome and that fibroelastosis represents its characteristic histological element.

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