A case of dissection of intracranial cerebral arteries with segmental mediolytic "arteritis"

A.C. ESKENASY-COTTIER, H.J. LEU, C. BASSETTI, J. BOGOUSLAVSKY, F. REGLI and R.C. JANZER

Abstract. The intravital diagnosis of intracranial arterial dissection is not always possible due to atypic and non-specific clinical and radiological presentations. The postmortem pathological examination of cerebral blood vessels is therefore necessary to establish or confirm the presence of a dissecting aneurysm of intracranial arteries. Most of the described cases showed no significant underlying vascular pathology. Here we present the case of a 24-year-old women who died 5 days after admission to the hospital for a rapidly developing right-sided hemisindrome. Neuroradiological examination had revealed ill-defined bifrontal hypodense lesions and angiographic findings were compatible with a dissection of the left extracranial internal carotid artery with embolic subocclusion of both anterior cerebral arteries. The pathological evaluation ruled out a thromboembolic occlusion of cerebral arteries and an extracranial internal carotid artery dissection but showed an extended dissecting process of variable age in the anterior circulation of the circle of Willis. The dissected vessels showed pathological changes characteristic of segmental mediolytic "arteritis" [Slavin and Gonzalez-Vitale 1976]. To our knowledge this is the first report on intracranial arteries being affected by this pathologic entity. Our case illustrates the importance of a postmortem examination of dissecting aneurysms of intracranial arteries. Careful serial section studies of dissected intracranial arteries in young subjects should be performed and may allow for a better understanding of the vascular pathology underlying the dissection processus.

Key words: cerebral arteries – dissecting aneurysms – arterial mediolysis – fibromuscular dysplasia

Received May, 14, 1993.

Correspondence to Dr. A.C. Eskenasy-Cottier, Institut de Pathologie, Division de Neuropathologie, Université de Lausanne, 27 rue Bugnon, CH-1005 Lausanne, Switzerland.
document multifocal rather than diffuse changes. We document the presence of lesions characteristic for a vasculopathy called segmental mediolytic "arteritis" [Lie 1992, Slavin and Gonzalez-Vitale 1976]. Although it is the first reported case in cranio-cerebral vessels it might be underdiagnosed due to its multifocal rather than diffuse nature.

Case report

Clinical data

This 24-year-old bank employee had an unremarkable family history. At the age of 9, and later from 17 to 20, she suffered from attacks of headache and seizure-like episodes, neurological and cardiovascular evaluation was normal. As a teenager she was treated for an anxiodepressive illness in a psychiatric indoor department. At the age of 19, she was suspected for hypothyroidism on the basis of obesity, hypsomnia, chills and amenorrhea, TSH was in the lower normal limit. Hypertriglyceridemia (3.2 mmol/l) was reported.

The week prior to admission she complained of headache, left carotidynia and general discomfort, and the night before suddenly presented somnolence, nausea, vomiting and involuntary movements of upper extremities, attributed to hashish consumption. At admission to the hospital she was somnolent, mutic, executed simple orders. General examination was unremarkable apart from a raised temperature of 38° C. White blood cell count was 12 G/l with 9% rods, sedimentation rate was normal. Gazometry showed a persistent normocapnic hypoxemia at 60 - 70 mm Hg. Toxicologic urinanalysis was positive for cannabis and barbiturates. EEG disclosed bilateral frontal slowing and cerebral CT scan 2 ill-defined hypodense non-enhancing expansive lesions, in the right frontal parasagittal convexity and the anterior part of left caudate nucleus. In the next few hours the patient became comatous, developing a slight right faciobrachiocrural hemisindrome, generalized hypertreflexia and bilateral Babinski's sign. Temperature raised to 39° C. CSF showed pleiocytosis with 7 cells/mm³ – 56% polymorphonuclear – and light hyperproteinorachia – 0.48 g/l. Bifrontal abscesses in the early stage were suspected and a broad-spectrum antibiotherapy started. A second CT scan disclosed a new hypodensity in the right caudate nucleus and a diffuse progression of prior lesions with mass effect. Cerebral angiography showed a flame-like tapering of the left cervical internal carotid artery (ICA) starting a few centimeters above the bifurcation and a subocclusion of both anterior cerebral arteries (ACA) with retrograde filling. Extracranial ICA dissection with embolic subocclusion of both ACA was diagnosed and intravenous heparin-therapy started. The next day, the third after admission, the patient presented a cardio-respiratory arrest, and died 36 hours after.

Fig. 1 Proximal right anterior cerebral artery (A1), 1.5 mm proximal to anterior communicating artery. Acute subintimal dissection with compression of the original lumen to about 50% by the false lumen. Irregular thickness of media with focal extensions of wall (thick arrows) at both edges of the dissected area, merging into a thinned segment. Thin arrows point to loose, increased collagen containing foci segmentally overlayed by a thickened intima (van Gieson elastic stain, x42).

Fig. 2 Right anterior cerebral artery, segment A2, 1.5 mm distal to anterior communicating artery. The expanded false lumen (asterisk) is focally externally limited by a wall devoid of media (upper left), reduced to a thin adventitia. Presence of a false microaneurysm (arrowhead). The non-dissected part of the vessel presents an irrugarily thick, collagen-enriched media overlayed by a thickened intima. Arrows point to altered intima. Note a dissected adjacent – orbitofrontal – branch (van Gieson elastic stain, x34).

General autopsy findings

Performed 48h post-mortem, general necropsy was unremarkable beside obesity, passive congestion of organs and the presence of fatty streaks in the aorta and its main branches. The carotid vessels in their extracranial portion were free of either dissection or thrombosis; they presented some atheromatous plaques and minor structural changes
A case of dissection of intracranial cerebral arteries

consisting of a variably thick tunica media showing loose, elastic-poor areas with foci of increased collagen and interspersed disorganized elastic lamellae.

Neuropathological findings

The circle of Willis and its major branches were dissected off the brain after fixation in 10% formalin. Brain was sliced in coronal plane. Sections of frontal, temporal, occipital and parietal cortex and white matter, basal ganglia, thalamus, midbrain, pons, medulla, cerebellum and of the vessels were embedded in paraffin and cut at a thickness of 8 µm. Serial step sections at intervals of 150 µm were taken of representative blocks. All were stained with hematoxylin-eosin, and selected ones with van Gieson-luxol fast blue, Prussian blue, von Kossa, van Gieson-elastin, alcian blue, Schiff periodic acid and reticulin as well as immunostained with a monoclonal anti-a-smooth muscle actin antibody.

The fixed brain weighed 1470 g and showed a marked generalized edema with bilateral uncal and necrotizing tonsillar hernia. Acute bilateral infarcts were present in the antero-medial part of the head of caudate nucleus and the adjacent portions of the internal capsule and putamen. A fresh hemorrhagic infarct extended antero-posteriorly along the right sulcus cinguli.

Histologically the presence of fresh infarcts was confirmed. They involved the territories of the left Heubner’s (a. recurrens) and lenticulo-striate (aa. centrales anterolaterales) arteries and of the right calloso-marginal artery. Focally more recent hemorrhagic components were present. In the territory of the right Heubner’s artery a less extended acute partial necrosis was observed. Microscopic examination of the different cerebral vascular areas showed further extended partial infarcts, limited on the right to regions supplied by cortical and ganglionic branches of anterior cerebral artery (ACA) whereas involving additional territories of the middle cerebral artery (MCA) on the left.

Superimposed on these focal lesions there was a generalized terminal anoxic encephalopathy. Intraparenchymatous vessels were normal apart from mineralizations of some vessel walls bilaterally in the pallidum and in leptomeninges in the region of the confluens sinuum.

The circle of Willis showed a classical configuration. Macroscopically both ACAs were suspect for an acute thrombosis. Microscopically an acute intramural dissection leading to various degrees of luminal narrowing was
Fig. 4 Higher magnification of Figure 3C. Segment of wall adjacent to the microaneurysm showing a transmural slit, the luminal orifice of which is flanked by a frayed elastic lamina (arrows), (van-Gieson elastic stain, ×170).

Fig. 5 Proximal left anterior cerebral artery, 0.65 mm proximal to anterior communicating artery. Subintimal dissection with disrupted internal elastic lamina floating in the lumen. Pronounced parietal alterations with markedly irregularly thick wall, protrusion of expanded intimal layer into the lumen, arrows point to foci of transversally cut smooth muscle fibers reflecting parietal disarraying (van Gieson elastic stain, ×42).

Fig. 6 Magnified view of serial section next to boxed area in Figure 5. Arrow points to focal inflammatory infiltrates in the vessel wall in an area almost devoid of media (immunostaining with monoclonal anti-α-smooth muscle actin antibody, ×106).

present, in both ACAs extending from their proximal origin to the pericallosal arteries, involving on the right the orbitofrontal, frontopolar and callosomarginal arteries. Despite serial sections we were not able to define the exact sites of entry and reentry of the dissection.

In the initial segment of right ACA the dissection followed a subintimal plane, with a false lumen compressing the original one to about 50% (Figure 1). The tunica media was irregularly thick with thinner segments containing areas of loosened smooth muscle content and increased collagen. In the portion following anterior communicating artery (ACoA), the vessel was distorted through an expansion of the false lumen. The dissection focally encom-

passed the whole media, covered by an undisturbed though focally dysplasia intima (Figure 2). Whereas on one edge of the dissection the wall showed medial and adventitial layers of various thickness enriched in collagenous tissue, on the other side it was devoid of media, composed of an altered intima and internal elastic lamina (IEL) and a fragmented, hemorrhagic adventitia. This pathological wall was contiguous to a false microaneurysm, presenting at its other neck’s pole with an abrupt interruption of media and IEL (Figure 3B). Serial sections through this portion of the vessel showed the proximal part of this microaneurysm to be in continuity with a segment of wall presenting a marked loss of media of varying depth, devoid of intima and forming an aneurysmal dilation (Figure 3A). Distally, the wall of the microaneurysm was gradually composed by a fibrocellular connective tissue (Figure 3C) which showed to merge into an adjacent thickened intima with a fragmented, frayed and irregularly thick IEL (Figure 3D). Further, the lesion had the aspect of a locally slightly distended vessel wall focally replaced by fibrous tissue underlying a thickened intima devoid of elastic lamina (Figure 3E). More distally it could be noticed as merging into a small focus of fragmented IEL covering a normal appearing media besides a discrete interposition of collagen (Figure 3F). At one place near the aneurysm (Figure 3C and 4) the wall presented a transmural slit. The more peripheral dissected branches of the vessel also showed multifocal parietal alterations involving both media and intima though without evident gaps or aneurysms.

The proximal left ACA (Figure 5) showed pronounced circumferential parietal alterations: a markedly irregularly thick media composed of disarrayed smooth muscle cells and focally increased collagenous tissue; a swollen or thinned, frayed, fragmented, interrupted IEL overlayed by an expanded subendothelial layer, at one point of the vessel protruding like a septum into the lumen.
A case of dissection of intracranial cerebral arteries

Fig. 7A and 7B  Anterior communicating artery. A: Vacuolization of vessel wall, internal elastic lamina (arrow) is forced into the lumen by a fresh hematoma. 7B: Swollen, vacuolated smooth muscle cells (arrows) intermingled with confluent, erythrocytes containing vacuoles (immunostaining with monoclonal anti-α-smooth muscle actin antibody; 7A x112, 7B x360).

The media was particularly thin at both edges of dissection. At one edge (Figure 6) in an area almost devoid of media a few polymorphonuclear leukocytes and lymphomonocytic cells were observed.

The anterior communicating artery was occluded through an organizing intramural hematoma. A striking vacuolization of the media extending over a segment of about one third of the total circumference was present. The vacuoles extended through the whole width of the media and were of various size, some contained erythrocytes, Most of the smooth muscle cells showed a swollen, vacuolated cytoplasm (Figure 7A, 7B).

The left supraclinoidal internal carotid artery was dissected too. The subintimal dissected area, extending into the middle cerebral artery (MCA), consisted of a richly vascularized granulation tissue, markedly reducing the lumen (Figure 8A, 8B). Alcian blue stained the thickened subendothelial layer; positive deposits could be seen in the IEL of both walls along the residual lumen and raising the IEL of the nondissected wall (Figure 10A).

The basilar and intracranial vertebral arteries showed alterations of intimal layer characterized by subendothelial fibroelastic thickening and irregularly thick, splitted IEL underlain and focally raised by small Alcian blue positive deposits (Figure 11A). Analogous though more pronounced alterations were found eccentrically on one third of the circumference of right middle cerebral artery (Figure 11B).

Discussion

This case illustrates the difficulty in clinically diagnosing intracranial arterial dissection, the angiographic aspect of which may be indistinguishable from a thromboembolic occlusion [Pessin et al. 1989]. The question may
be raised whether a proportion of cases diagnosed as extracranial carotidal dissection with distal embolization might actually correspond to intracranial dissection and that this diagnosis might be underdiagnosed.

The presence of granulation tissue areas older than two weeks in the left supraclinoidal and middle cerebral arteries of our patient reaffirms the occurrence of clinically silent intracranial arterial dissections, relevant considering the generally accepted view of severe prognosis linked with this condition, pointing to the evoked implication of other contributing factors than the dissecting process per se [Farrell et al. 1985].

Taken together these considerations reinforce the suspicion of intracranial arterial dissection as being underdiagnosed and point to the need for detailed pathological evaluation of cerebral vessels. The latter further allowed in the present case to diagnose an underlying vasculopathy consistent with segmental mediolytic "arteritis" (SMA).

Slavin and Gonzalez-Vitale 1976 report a type of lesion they term SMA. They describe in 3 autopsy cases arterial lesions in large visceral abdominal arteries and the distal portion of renal arteries, consisting of a variable thickness of the tunica media with a focal and segmental loss of smooth muscle cells leading, when associated with intima and elastica dissolution, to the formation of parietal gaps or to dissecting aneurysms. Some gaps are covered by fibrin deposits, externa elastica and adventitia, others are filled with granulation tissue or thrombi, occasionally they evolve into saccular aneurysmal dilation which may rupture. Fibrin deposits are visible at the junction of outer media with external elastica in acute lesions without any significant cellular inflammation in most of them. Partial medial defects are generally replaced by loose fibrous tissue frequently containing neovessels which may rupture, leading to a longitudinal dissection. Additionally in the tunica media a focal increase of medial ground substance and foci of collagenization are found in areas where smooth muscle fibers are degenerating or totally disappeared. The authors describe the latter alterations in terms of medial degenerative changes distinguishing them from the first which they call destructive, leaving the question of a relation between the two open.
In 1989 Slavin et al. report on 2 additional cases, one again in visceral abdominal muscular arteries of a 87-year-old man, the other in the epicardic coronary arteries of a 37–38 week-old neonate with hyaline membranes disease. In addition to and with or without fibrin deposition, focal extravasation of erythrocytes may be seen, at the mediodiventitial junction but also within the media and mediodiletic areas. Apparently occurring at the mediodiventital junction, also involving the mid and inner media, the lytic process is ultrastructurally characterized by the transformation of the arterial smooth muscle cytoplasmic content into a maze of dilated vacuoles containing oedema-like fluid, their rupture disrupting the smooth muscle cells, completing the mediodiletic process. Vacuolar formation is noted in adjacent endothelial cells. The extracellular matrix is focally expended, containing fibrin, fragments of elastic, smooth muscle derived vacuoles, platelet thrombi. Areas of lysed media are replaced by expanded extracellular matrix material containing dilated vascular spaces, and presumed more advanced or healed lesions replacing the arterial wall consist of a ground substance, cell-poor layer applied on an elastic lamina deriving from both interna and externa elasticas. A careful study of the literature done by the same authors indicates that lesions virtually identical to SMA have been described in coronary arteries of neonates [De Sa 1979; Gruenwald 1949].

Two more cases have since been published, one by Heritz et al. 1990 in the large omental arteries of a 68-year-old man, another by Armas and Donovon 1992 in medium-sized and small branches of hepatic arteries of a 75-year-old female.

The pathological findings in our case fit the diagnostic features of SMA: extended intracellular and erythrocytes containing extracellular vacuolization of the wall circumference of ACoA, focal medial replacement through not yet organized fibrinous and erythrocytic elements or intramural neovessels in the dissected area of left supracraildinal ICA and MCA, areas of segmental mediolysis varying from focal wall thinning to gap and microaneurysm in both dissected ACAs.

We did not observe mediol ground substance accumulation as described by Slavin and Gonzalez-Vitale in their first 3 patients as a degenerative condition linked or not with SMA or as end-stage lesions in their ulcerated paper, however, Alcian blue positive deposits were present sub-intimally, in the dissected vessels as well as in the vertebro-basilar system, extensively overlayed by altered intima and elastica, rather recalling of the lesions described by De Sa [1979] in his older infants. Whether they reflect secondary changes to a mediolytic process extending to intima or a primary lesion of intima susceptible of rupture, dissection and subsequent healing or scarring cannot be ascertained.

Aging, leading to intimal alterations as those observed here, is not reported to be associated with focci of subintimal ground substance accumulation. Moreover, among different arterial territories, cerebral arteries would present with less aging signs than coronary arteries, which were normal in this young patient, further, at the cerebral level, aging presents with medial fibrosis, sparing for a long time intima and IEL [Boissou et al. 1987].

Alcian blue positive deposits have been described in the media of arteries in cases of mucoid media degeneration [Anderson and Schechter 1959, Boström and Liliequist 1967, Bradac et al. 1981, Brice and Crompton 1964, Leu 1988, Lloyd and Bahnsen 1971, Thapedi et al. 1970] and in cases of fibromuscular dysplasia (FMD) of medial fibroplasia type. These deposits were particularly pronounced in the areas of fibromuscular ridges, evoking for some authors [Sato and Hata 1982] that a dissection might occur at a transitional portion between the areas of extreme mural thinning and thickened fibromuscular ridges, and extend along the structural weakness caused by mucin pools. The findings in our case fit well with this proposed mechanism for the extension of dissection along a weakened subintimal plane. Since we have, as in the other described cases, only a very limited presence of inflammatory cells, easily interpretable as reactive to the dissection, we feel, as other authors [Armas and Donovan 1992, Heritz et al. 1990, Lie 1992, Slovin et al. 1989] that the term "arteritis" is inappropriate and should be replaced by "arteriopathy".

Some features of our cases show parietal alterations compatible with FMD, though without prominent fibrosis and difficult to classify in one of the pathological types of this affection [Camilleri 1987, Harrison 1971, Lüscher 1987]. In left ACA (Figure 5) the lesions involved the medial and intimal layers; in the vertebro-basilar and right middle cerebral arteries they might be compatible with the intimal fibroplastic type. This partial overlap of SMA and FMD is also discussed by Lie who considers SMA to be a variant of FMD. The rarity of histopathologically documented cases of intracranial FMD does however not allow to draw conclusions about the exact relationship between SMA and FMD. Up to 1984 10 cases of histopathologically documented intracranial FMD have been reported [Abdul-Rahman et al. 1978 cases 3 and 4, Hartman et al. 1971, Hegedüüs and Németh 1984, Hirsch and Roessmann 1975, Kalyanraman and Elwood 1980, Kalyanraman et al. 1983, Pilz and Hartjes 1976, Pollock and Jackson 1971, Rinaldi et al. 1976] among which 3 with dissection [Hegedüüs and Németh 1984, Hirsch and Roessmann 1975, Pilz and Hartjes 1976] and 4 with marked intimal changes. Bellot et al. 1985 studied a case of widespread FMD in a normotensive 40 year-old woman involving cervico-cephalic arteries with intracranial extension not demonstrated angiographically, describing FMD lesions, multiple mural dissections, some of which resembling to the slit shown in Figure 4, saccular aneurysms or outpouchings. The authors classify their case in the fibroplastic type of medial FMD, attributing the associated intimal thickening to secondary circulatory disturbances caused by the FMD and the dissections.
If one takes into consideration that intracranial vessels lack vasa vasorum with the exception of cases with severe atherosclerosis [Hegedüs 1985, Stehbens 1972], the only source of an intramural hemorrhage is the vessel lumen. This might explain the apparent lack of primary mediodventitial involvement in our case, the lesions being situated at the more luminal side of the vessel. The dissection in SMA is therefore secondary to a primary pathological process in the media and intima. This does not speak against the suspected pathological role of hypoxemia or shock clinically encountered as a common denominating factor in all SMA cases including ours.

In conclusion we present the case of an intracranial dissecting aneurysm in a young woman with an underlying vasculopathy fulfilling the criteria of SMA. This case stresses the importance of a detailed postmortem examination of intracranial vessels in order to establish the true incidence and nature of this probably underdiagnosed entity.

Acknowledgements

We thank Drs M. Lasserre-Baum, E. Héraüef, O. Karkayannis and S. Zagury for helpful informations about the medical history of the patient. We are grateful to Prof. J. Schneider for his comments on the pathological findings.

REFERENCES


Bogousslavsky J, Despland PA, Regli F 1987 Spontaneous carotid dissection with acute stroke. Arch Neurol 44: 137-140

Bogousslavsky J, Regli F 1987 Ischemic stroke in adults younger than 30 years of age, cause and prognosis. Arch Neurol 44: 479-482


Bousser MG, D'Anglejan J 1991 Dissection des artères cervico-céphaliques. La Presse médicale 20: 729-731


Caplan LR 1986 Miscellaneous cerebrovascular conditions. Semin Neurol 6, 3: 267-276


De Sa DJ 1979 Coronary arterial lesions and myocardial necrosis in stillbirths and infants. Arch Dis Child 54: 918-930


Gruenwald P 1949 Necrosis in the coronary arteries of newborn infants. Am Heart J 78: 889-897


Hedegås K 1985 Reticular fiber deficiency in the intracranial arteries of patients with dissecting aneurysm and review of the possible pat­hogenesis of previously reported cases. Eur Arch Psychiatr Neurol Sci 235: 102-106


A case of dissection of intracranial cerebral arteries


Manz HJ, Vester J, Lavenstein B 1979 Dissecting aneurysm of cerebral arteries in childhood and adolescence; case report and literature review of 20 cases. Virchows Arch A Path Anat and Histol 784: 325-335


Stehbens WE 1972 Pathology of the cerebral blood vessels. Mosby, Saint Louis


Youl BD, Bousser MG, Mas JL 1988 Dissections des artères intracrâniennes. Artères et veines. 7: 421-425