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AJNR Am J Neuroradiol 1982, 3 (5) 572-576

<http://www.ajnr.org/content/3/5/572.citation>

This information is current as
of April 23, 2024.

Neurofibromatosis with Extensive Intracranial Arterial Occlusive Disease

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Neurofibromatosis produces a broad spectrum of clinical manifestations as a result of widespread dysplasia of mesodermal and neuroectodermal tissues [1]. One of the more serious aspects of the disease relates to the arterial involvement that may occur. Renal arterial disease with resultant hypertension has been particularly well documented. However, a number of reports have also documented the extensive intracerebral arterial abnormalities that may occur.

Since the description in 1971 by Hilal et al. [2] of three children with neurofibromatosis and cerebral arterial disease, a number of other case reports have substantiated this aspect of the affliction. Most of the reports have concerned patients in childhood or adolescence. In 1976, Tom-sick et al. [3] reviewed 12 previously reported cases and presented two more case reports with cerebral involvement. To our knowledge, there has been no report in which the arterial changes over a long period of time have been documented by serial angiography. We report an adult patient with neurofibromatosis and intracerebral arterial involvement who had two angiographic evaluations spaced 12 years apart.

Case Report

Twelve years before admission to Mount Auburn Hospital, a 52-year-old, mildly retarded woman had presented to an outside hospital with the chief complaint of severe headaches over a 5 day period. The patient had been diagnosed in childhood as having neurofibromatosis on the basis of widespread cutaneous neurofibromas and café-au-lait spots. At that time, she was mildly confused and uncooperative and had bilateral quadriceps clonus and an inability to look upward or to either side. The rest of the neurologic examination was normal, and lumbar punctures showed evidence of subarachnoid bleeding with about 50,000 red blood cells/mm³.

A right carotid arteriogram had demonstrated a small internal carotid artery with a severe stenosis of the terminal part of the siphon (fig. 1A). There was extensive collateral flow to the frontal and parietal distribution via enlarged middle meningeal collaterals. A left carotid arteriogram had demonstrated similar changes in the internal carotid artery with extensive collateral flow about the base

of the brain. A deep seated aneurysm (figs. 1B and 1C) in the region of the left thalamus was shown, probably arising from the posterior choroidal artery. An avascular area around the aneurysm was thought to be a hematoma. In view of its peripheral location, the possibility of a mycotic aneurysm was raised but multiple blood cultures subsequently showed no growth. The findings from this admission were briefly mentioned but not illustrated in a previous report [4]. After 1 month of supportive therapy, she was discharged and essentially returned to her baseline status.

After her discharge, there was very little change in her overall status for 12 years. About 12 years after the initial episode, at age 64, she presented to the Mount Auburn Hospital for emergency evaluation because of a sudden onset of obtundation after episodes of coughing. On admission, she was somnolent and could be aroused in response to her name. Other than the obtundation and lack of volitional movements, physical examination revealed no change from her baseline, again demonstrating a mild left hemiparesis and extensor left plantar reflex. Chest radiography demonstrated a right lower lobe pneumonia, and laboratory data showed an elevated white blood cell count of 15,000/mm³ with a shift to the left. Lumbar puncture again demonstrated grossly bloody cerebrospinal fluid (CSF) with a CSF hematocrit of 12% (peripheral hematocrit of 40%).

An emergency angiogram of the right carotid artery demonstrated a small internal carotid artery from its origin to the level of the anterior clinoids, above which the internal carotid artery was markedly and smoothly stenotic (fig. 2A). There was only very minimal direct filling of the middle and anterior cerebral artery with extensive collateral flow via the external carotid artery branches, particularly enlarged middle meningeal collaterals. There was a deep-seated network of small collateral vessels. The appearance of the left carotid arteriogram was quite similar (figs. 2B and 2C). The vertebral arteriogram demonstrated no abnormality in the posterior fossa arteries, but collateral flow from the posterior cerebral arteries to the anterior and middle cerebral arteries was present (fig. 2D). There had been essentially no change in the extensive intracranial abnormalities since the angiogram 12 years previously except for some questionable decrease in the very minimal direct middle cerebral filling that had been present on the original study. However, the left posterior choroidal aneurysm was no longer demonstrable.

Computed tomographic (CT) scans showed no evidence of intracranial hemorrhage, although the first of the CT scans was per-

Received November 30, 1981; accepted after revision April 5, 1982.

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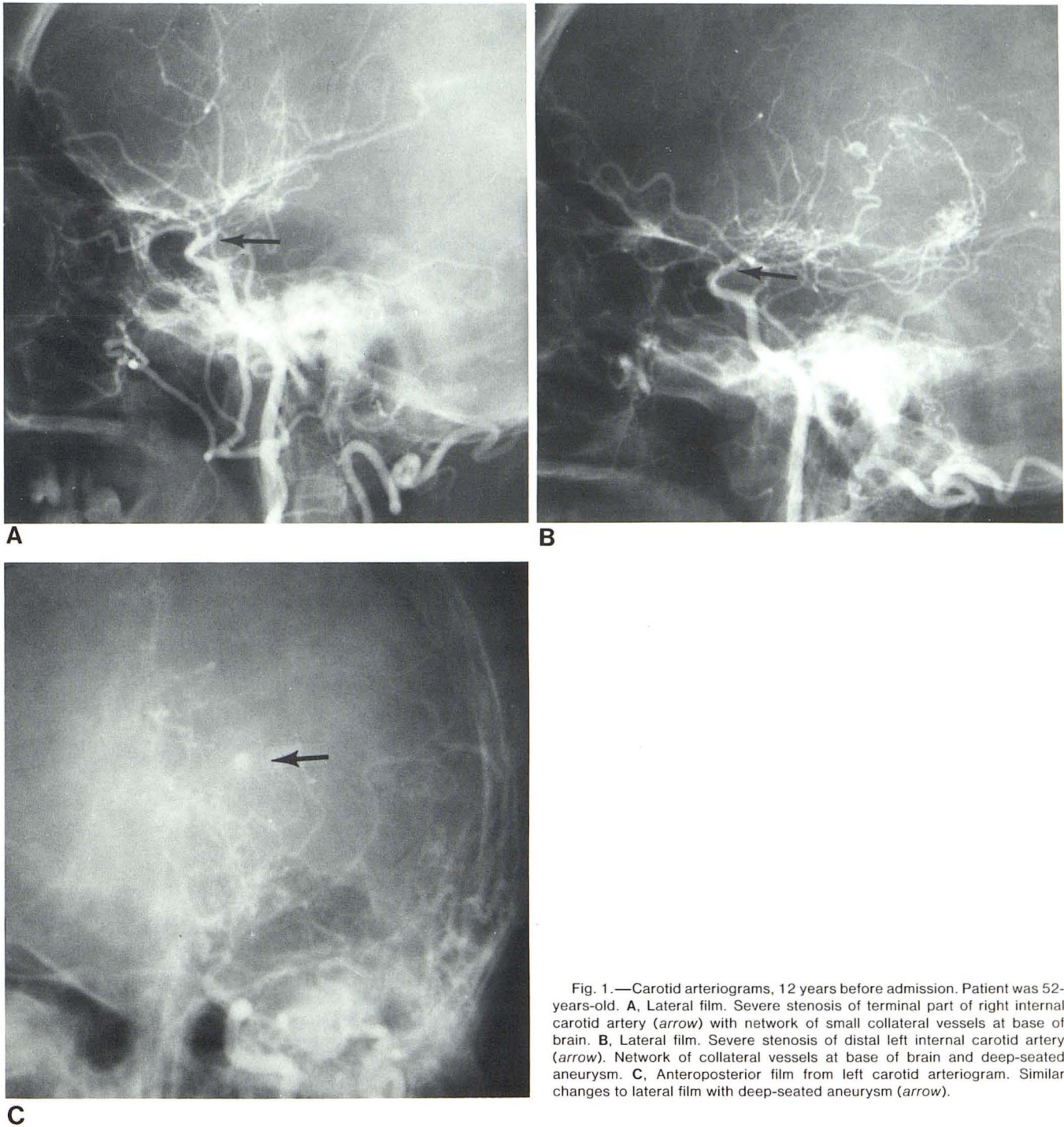


Fig. 1.—Carotid arteriograms, 12 years before admission. Patient was 52-years-old. **A**, Lateral film. Severe stenosis of terminal part of right internal carotid artery (*arrow*) with network of small collateral vessels at base of brain. **B**, Lateral film. Severe stenosis of distal left internal carotid artery (*arrow*). Network of collateral vessels at base of brain and deep-seated aneurysm. **C**, Anteroposterior film from left carotid arteriogram. Similar changes to lateral film with deep-seated aneurysm (*arrow*).

formed 9 days after the acute event. Progressive hydrocephalus developed and improved after a shunt procedure. However, the patient continued to be unable to perform volitional movements and despite antibiotic and steroid therapy, she died 5 weeks after admission. Postmortem examination was not performed.

Discussion

Although extensive disease of the intracerebral arteries has been demonstrated by arteriography in patients with

neurofibromatosis, microscopic evaluation of the arterial disease has been primarily limited to the renal arteries and, less often, the aorta and its other intraabdominal branches. The characteristic angiographic pattern of renal artery involvement is long segments of smoothly tapered stenosis [5]. The renal artery involvement is characterized by various degrees of intimal thickening due to proliferation of spindle cells or fibrous thickening, thinning of the media, and fragmentation of the elastica. The latter finding has been associated with small aneurysms [6].

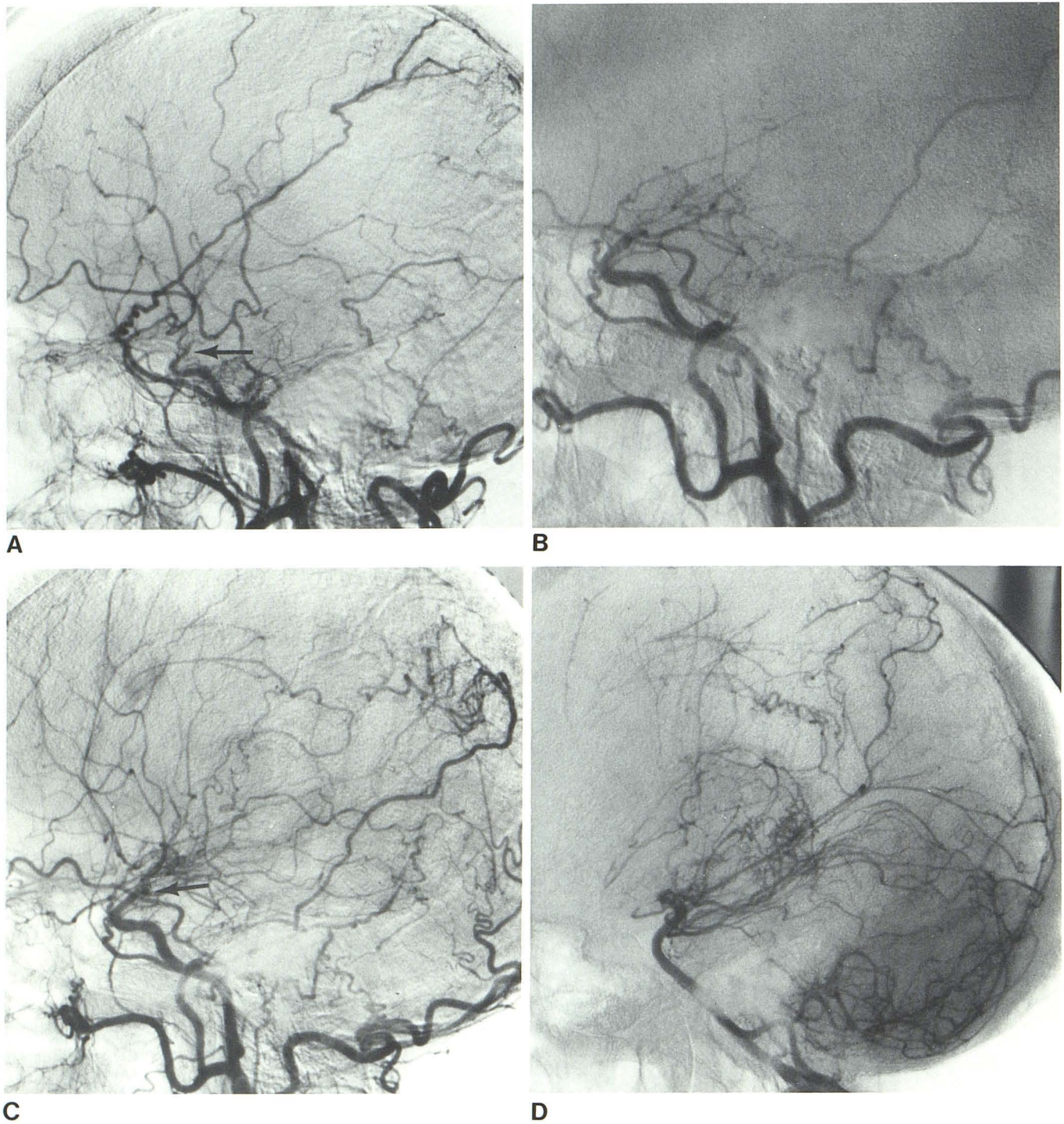


Fig. 2.—Lateral films; patient, age 64. A–C, Carotid arteriograms. A, Small right internal carotid artery with severe stenosis at distal siphon (*arrow*). Poor direct filling of anterior and middle cerebral arteries and large external carotid vessels with collateral transdural flow. B and C, Small left internal carotid artery with severe stenosis of distal siphon (*arrow*). Poor direct filling

of anterior and middle cerebral arteries and large external vessels with collateral transdural flow. Network of collateral vessels at base of brain. D, Vertebral arteriogram. Normal posterior fossa vessels and posterior cerebral artery. Extensive collateral flow from posterior cerebral artery and its deep-seated branches.

Unlike the well established microscopic findings of renal artery disease in neurofibromatosis, there is only a single published case of autopsy findings of diseased intracerebral vessels. In 1978, Lamas et al. [7] reported a case of a 50-

year-old man who presented with sudden onset of headache followed by seizures and left hemiplegia [7]. The CSF was bloody, and angiography demonstrated the typical pattern of bilateral incomplete occlusion of the supraclinoid carotid

artery with an associated vascular network at the base of the brain. Microscopically, there was "concentric luminal stenosis (about 50%)" of the intrapetrous parts of both carotid arteries. However, at a supraclinoid level, these arteries appeared "hypoplastic without luminal stenosis." Intimal hyperplasia with fragmentation of the elastic layers was also demonstrated. Similar intimal hyperplasia was also demonstrated in a middle cerebral artery and in small-sized pulmonary, pancreatic, and renal arteries. It is also of interest that the vertebral, basilar, and posterior cerebral arteries were enlarged but otherwise normal in appearance. The microscopic findings of the intracerebral arteries in this single case are thus similar to those that have been described in the systemic vessels.

It is remarkable that in the reported cases of neurofibromatosis with intracranial arterial occlusive disease that stenotic or telangiectatic involvement of the vertebral, basilar, and posterior cerebral arteries has only been described once [8]. Further, absence or stenotic or telangiectatic involvement of the posterior circulation seems to be a common feature of many conditions associated with intracerebral arterial occlusion and an arterial network at the base of the brain described by various authors as "collateral network," "basal telangiectasia," or "moyamoya" vessels. This includes the idiopathic form, termed "moyamoya," characteristically occurring in females before 20 years of age and presenting with sudden onset of focal motor deficit or convulsions. A remitting course is characteristic [7, 9]. The same angiographic pattern of altered anterior and normal posterior circulation occurs in those cases of basal arterial occlusions attributed to many other factors including meningitis [2, 6], embolism [2], other neurocutaneous syndromes [2], overtransfusion [10], sickle cell anemia [11], and slowly growing brain tumor [12].

Our patient with a basal arterial occlusion had an aneurysm supplied by the posterior choroidal artery that was present on the initial study but not demonstrated on the latter examination. In 1978, Kodama and Suzuki [13] reported five cases of intracerebral aneurysms in a series of 56 moyamoya patients (21 children and 35 adults). All five were adults. Three of the five aneurysms occurred at the peripheral part of the posterior choroidal artery. Because of the location and the disappearance of the aneurysm on follow-up angiography, the authors concluded that they were not true aneurysms but pseudoaneurysms indicating the bleeding point in the brain tissue. They also postulated that decreased flow through the anterior circulation due to the progressive stenosis leads to increased posterior circulation flow. The increased flow is presumed to cause preexisting areas of weakened arterial media to undergo aneurysmal dilatation and/or rupture. Although our case is one of neurofibromatosis rather than moyamoya syndrome, the proposed mechanism seems equally pertinent. A recent review of 23 patients with aneurysms associated with moyamoya disease demonstrated that 43.3% of the aneurysms developed in the posterior circulation [14]. In this report from Japan, subarachnoid hemorrhage was the initial presentation in 84% of cases, attributable to rupture of the aneurysm in nine cases, breakdown of moyamoya vessels

in five cases, both types in one case, and unknown in five cases. In another recent report [15], magnification angiography demonstrated an aneurysm in four of seven patients with moyamoya. It is remarkable that despite the extensive involvement of the anterior cerebral circulation, our patient had a striking lack of focal neurologic findings and that the two catastrophic events, separated by 12 years, were subarachnoid hemorrhages with confirmed positive findings in the posterior circulation during the first episode.

Most of the cases of intracerebral vascular involvement with neurofibromatosis have been described in children or young adults without long-term follow-up. In patients with moyamoya disease, angiographic evaluations over a period of up to 5 years have been reported, with emphasis on the progressive development of the collateral basal network during the period of observation [9, 16, 17]. Other authors have stressed that moyamoya tends to progress in attacks but that the progression may cease at any stage [17].

Our case represents the only reported experience with intracerebral arterial occlusive disease in a patient with neurofibromatosis evaluated over a 12 year interval. While the relative lack of significant change in the extensive arterial disease over 12 years is of interest, more experience with other patients with neurofibromatosis—and particularly younger patients—will be necessary before it is possible to formulate more definite opinions regarding long-term prognosis when the extensive arterial changes are seen in their more usual setting of a child or young adult.

ACKNOWLEDGMENT

We thank Juan M. Taveras for permission to publish films from the Massachusetts General Hospital.

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