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Non-Penetrating Trauma to the Carotid Artery With Secondary Thrombosis and Embolism: Treatment by Thrombolysin

By

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With 3 Figures

Summary

A case of partially occluding post-traumatic thrombosis of the internal carotid artery and secondary embolism of the middle cerebral artery is reported. The patient was treated with Thrombolysin with coincident resolution of clinical symptoms and signs and clearing of the lesions on arteriography. This may have been fortuitous.

The subject of traumatic carotid artery thrombosis is reviewed in detail, and its pathophysiology is discussed, especially in relation to facts known about occlusive vascular disease secondary to atherosclerosis and related embolic phenomena. Suggestions are made concerning the treatment of this condition, especially with regard to developing rational criteria for opening vascular beds through evaluation of collateral cerebral blood flow. The uses of microvascular surgical techniques and thrombolytic therapy are considered.

Non-penetrating trauma to the internal carotid artery resulting in thrombus formation is a fairly rare, though well-reported problem. When the occlusion is subtotal, and when emboli are noted, the condition is especially unusual. We recently cared for a patient with post-traumatic partial carotid thrombosis and cerebral embolism. After employing thrombolytic therapy, we observed clinical and angiographic improvement, which may have been fortuitous. This is the first time thrombolysis has been attempted for such a problem. A review of the literature revealed a number of interesting features of post-traumatic carotid thrombosis and possibilities for treatment. One point which must be emphasized is that the principles regarding the treatment in all cerebrovascular occlusive disease of whatever aetiology must be the same.

Case Report

Arizona medical college 0817-73-4: The patient, a 31 year old right-handed jockey, allegedly fell from a horse and had an immediate seizure. He arrived at the emergency room forty minutes later. Although he did not remember his accident, he was intact neurologically. He had a fracture of his right first metacarpal, which was splinted. X-rays of the skull and cervical spine were normal.

Six hours later, while under observation, he suddenly developed moderate decrease in level of consciousness with deviation of gaze to the right and a profound spastic left hemiparesis. He was immediately given 100 mg of Decadron intravenously and 750 cc of 20% mannitol. Transfemoral cerebral arteriography was performed at once and demonstrated a partial occlusion of the cervical portion of the right internal carotid artery secondary to an intraluminal thrombus and an extraluminal hematoma. There was also a complete occlusion of the right middle cerebral artery at its origin (Fig. 1). Leptomeningeal flow was seen to supply the middle cerebral artery branches on delayed serial filming (Fig. 2).

A stellate ganglion block was performed on the right. Intravenous "Thrombolysin" was begun with 100,000 units given immediately followed by 50,000 units every six hours for three days. The patient received a total of 700,000 units. The prothrombin time did not change appreciably, but the haemoglobin dropped from 15.1 gm% to 11.0 gm% in five days. Within twelve hours the patient could look to the left on command, and within twenty-four hours he began voluntarily to move his left limbs. From that time on he continued to have slow but steady neurological improvement. Four days after the injury a repeat transfemoral right common carotid arteriogram demonstrated resolution of the middle cerebral artery embolus with a normal perfusion pattern of the right middle cerebral artery branches. The internal carotid artery thrombus was felt to have resolved, although an extraluminal defect, presumably a haematoma, persisted (Fig. 3).

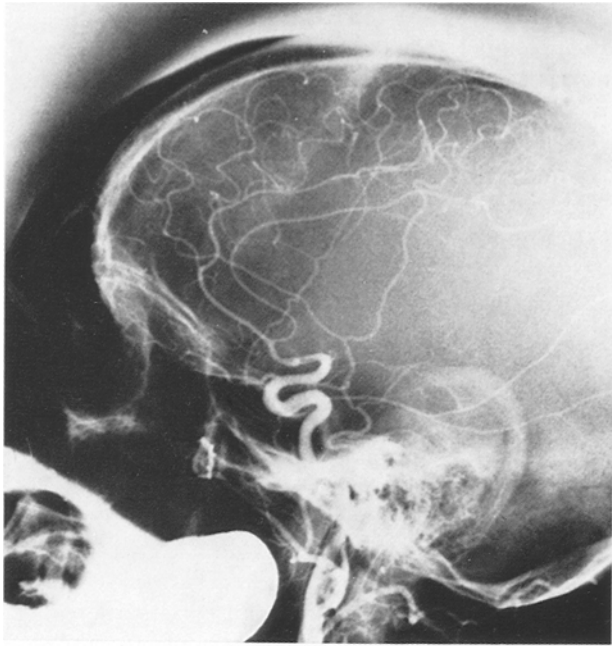
On discharge, three weeks after injury, the patient's left motor function appeared to be almost normal. He seemed to have some decrease in intellectual function, and impairment of judgment. He did not keep follow-up appointments.

Discussion

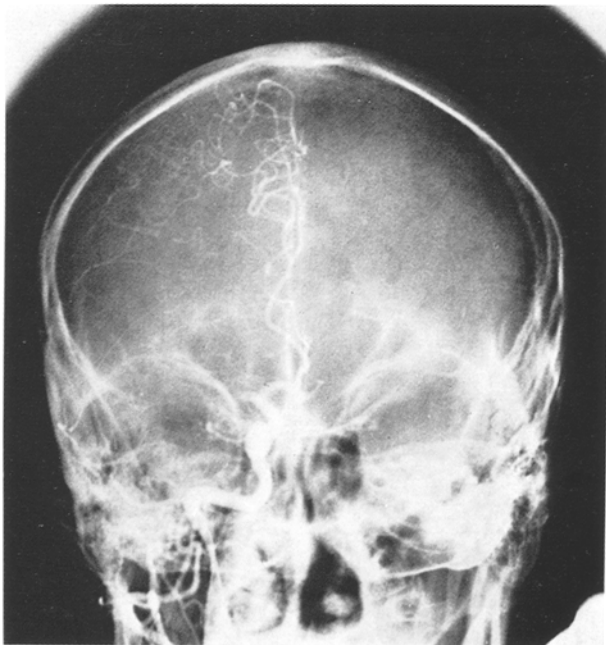
1. Clinical Aspects

There have been approximately 50 articles in the English literature in the last forty years dealing with non-penetrating trauma to the internal carotid artery with secondary thrombosis. These include a number of extensive and thoughtful reviews, some of which refer to the non-English literature, and in which up to 115 cases have been accumulated (Fleming and Petrie 1968, Garg *et al.* 1968, Gleave 1966, Horner *et al.* 1970, Jernigan and Gardner 1971, Little *et al.*

Fig. 1. Initial right common carotid arteriogram. a Lateral: Note lack of perfusion in middle cerebral artery distribution and thrombus in the extracranial portion of the right internal carotid artery. b AP: Note embolus in proximal portion of right middle cerebral artery and extrinsic pressure deformity along lateral aspect of extracranial internal carotid artery secondary to haematoma



a



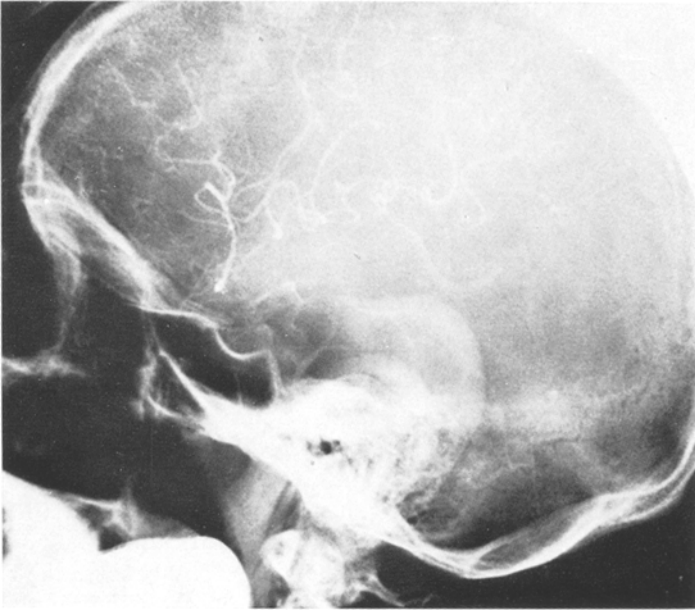
b

1969, Mastaglia *et al.* 1971, New and Momose 1969, Schneider *et al.* 1971, Sullivan *et al.* 1973, Towne *et al.* 1972, Verbiest and Calliauw 1959, Yamada *et al.* 1967, Zilka 1970).

A typical clinical picture of symptoms and signs has been described, and certain variations have been noted. The patient, usually a young man, presents after an automobile accident or altercation with a history of head injury and, less frequently, with an associated neck injury. If the head injury has been severe, as in the case of 25% of the patients (Fleming and Petrie 1968, Yamada *et al.* 1967), this may direct attention away from the vascular system. The usual range of problems of cerebral contusions, deep structure dysfunction, and hematomas may be seen. Thus the diagnosis of vascular injury may be difficult, and, indeed, the correct diagnosis has rarely been made clinically. If the head injury has been mild, there may be a lucid interval of hours to days before symptoms occur. Initial symptoms may be those of transient ischaemic attacks. The symptoms and signs are most frequently those of a hemispheric deficit with most severe dysfunction in the territory of the middle and possibly anterior cerebral arteries. There may be evidence of increased intracranial pressure. In many cases there is a relative preservation of an excellent level of consciousness, above that to be expected in a head injury with hemispheric symptoms.

Damage to other local structures can be suggestive that carotid injury may also be present. Injury to the sympathetic chain can occur and can be expressed as a Horner's syndrome (Fleming and Petrie 1968, Jernigan and Gardner 1971, Lewin 1968). Jaw fractures are often seen (Berman 1975, Caldwell and Hadden 1948, Garrison *et al.* 1975, Hughes and Brownell 1968, Miller and Ayers 1967, Salmon and Blatt 1968, Schneider *et al.* 1971, Silvernail *et al.* 1975, Sullivan *et al.* 1975, Toakley and McCaffrey 1965, Zilka 1970). Shoulder fractures or evidence of chest trauma can be seen (Garg *et al.* 1968, Gleave 1966, Schneider and Lemmen 1952, Schneider *et al.* 1971), suggesting that the carotid artery may have been stretched. Spinal fractures have also been seen (Houck 1964, Lai *et al.* 1966, Zilka 1970). Basilar skull fractures may include the region of the carotid canal, the anatomy of which has some importance (Yashon *et al.* 1964), and can cause secondary damage to the carotid artery (Garg *et al.* 1968, Schneider *et al.* 1971, Sedzimir 1955, Thompson 1963,

Fig. 2. Initial right common carotid arteriogram. a and b Lateral and AP: Delayed phase of initial examination demonstrating perfusion of middle cerebral artery group via leptomeningeal collaterals



a



b

Yashon *et al.* 1964, Zilka 1970). Recently, it has been noted that basilar skull fractures may be seen in mild head injury and may occur at a distance from local trauma (Hirsh and Kaufman 1975).

Carotid thrombosis is indicated when there is a decrease of the carotid pulsation in the tonsillar region (Dunning 1953). However, the pulsation may not be decreased with occlusion, since it may be transmitted from the external carotid artery (Garg *et al.* 1968, Rosegay 1956) or along the occluded vessel. Decreased pressure on ophthalmodynamometry may be suggestive of carotid thrombosis (Gleave 1966, Schneider and Lemmen 1952), though, even with an occluded vessel, it may be normal (Johnson and Walker 1951).

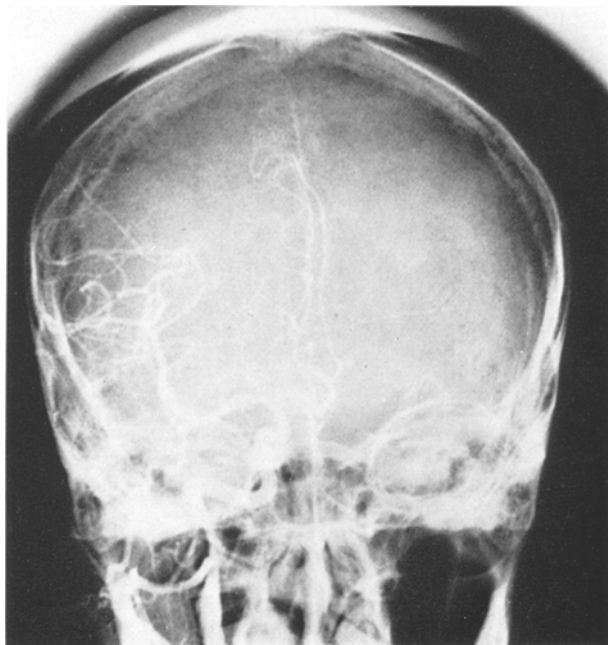
Definitive diagnosis is usually not made until arteriography. In most cases, a complete occlusion is seen (New and Momose 1969) though stenotic lesions have been observed (Bickerstaff 1964, Frantzen *et al.* 1961, Friedenberg 1973, Garg *et al.* 1968, Gleave 1966, Horner *et al.* 1970, Miller and Ayers 1967, Salmon and Blatt 1968, Schneider *et al.* 1971, Sullivan *et al.* 1975, Yamada *et al.* 1967). Where a subtotal occlusion is noted, a traumatic thrombus may be differentiated from atherosclerosis on angiography because the region involved in the former is usually long and involves the middle and distal thirds of the cervical internal carotid artery (Miller and Ayers 1967), while the latter generally occurs at the carotid bifurcation. A gradual narrowing may indicate that the initial obstruction was high (Zilka 1970).

In one series of 10,000 head injuries, the incidence of carotid thrombosis was 0.2% (Gleave 1966). It is noteworthy that trauma is the most common of known causes of internal carotid artery occlusion in young adults (Humphry and Newton 1960). In a review of carotid occlusion in children and adolescents, 25% of the recorded cases up to 1966 were due to trauma (Pitner 1966). In one series of 7,000 arteriograms, 140 cases of stenosis and occlusion of the internal carotid artery and its branches were noted. Of these, 13 were secondary to trauma (Momose and New 1973). In another series, 3 of 27 internal carotid occlusions were related to trauma (Jacobsen and Skinhoj 1957). In only two cases have bilateral occlusions been seen (Ojeman and Moser 1964, Yashon *et al.* 1964). The condition is

Fig. 3. Follow-up right common carotid arteriogram. a Lateral: Normal perfusion of right middle cerebral artery distribution. b AP: Resolution of middle cerebral artery embolus. Note continued extrinsic pressure on the internal carotid artery secondary to cervical haematoma. (Apparent right to left midline shift is accounted for by slight rotation of the patient's head)



a



b

being recognized more frequently since arteriography is being used more aggressively in head injuries (Carton 1959, Verbiest and Calliauw 1959).

2. Pathophysiology

The pathophysiology of intravascular thrombosis secondary to trauma seems straightforward. It is well known that thrombus will form wherever there is intimal disruption with exposure of the subintimal tissues (Sherry *et al.* 1969). Two factors dispose to intimal disruption. First, the intima is the least elastic layer of the vessel wall and will tend to crack when the vessel is deformed (Gleave 1966). Second, one natural plane of separation in the vascular system is between the intima and the media. Thus, intimal disruption could be expected to occur from trauma and provide the substrate for thrombus formation. In operative observations and pathological examinations, intimal disruption has indeed been seen in a number of patients (Caldwell and Hadden 1948, Clarke *et al.* 1955, Dratz and Woodhall 1947, Fletcher *et al.* 1974, Gleave 1966, Gurdjian *et al.* 1963, Horner *et al.* 1970, Lewin 1968, Linell and Tom 1959, Little *et al.* 1969, MacKintosh 1965, Murray 1957, Northcroft and Morgan 1944, Ritchie 1961, Verbiest and Calliauw 1959, Yamada *et al.* 1967, Zilka 1970). Where this was not obvious, either the search was possibly not extensive enough, or a small disruption may have been overlooked.

Disruption could occur due to two causes, either direct injury or stretching. The direct application of forces with non-penetrating injuries has been presumed in a fair proportion of the cases. Indeed, the carotid has been injured by manipulation by physicians, as in testing for carotid sinus hypersensitivity (Calverley and Millikan 1961, Nelson and Mahru 1963) or during surgery (Calverley and Millikan 1961, Linell and Tom 1959). In missile wounds without direct injury, forces transmitted against the vessel wall have also resulted in thrombosis (Caldwell and Hadden 1948, Clarke *et al.* 1955, Frantzen *et al.* 1961, Gurdjian *et al.* 1963, Linell and Tom 1959, Little *et al.* 1969, Murray 1957, Northcroft and Morgan 1944, Raney 1948, Zilka 1970). Blunt trauma can also be delivered to the carotid artery in intraoral injuries since the artery lies close to the surface of the tonsillar fossa (Bickerstaff 1964, Braudo 1956, Caldwell 1936, Fairburn 1957, Miller and Ayers 1967, Pitner 1966, Scott *et al.* 1960, Shillito 1964).

Force could also be applied along the long axis of the vessel by stretching by rotation or extension of the neck (Garg *et al.* 1968, Gleave 1966, Horner *et al.* 1970, Lewin 1968, Little *et al.* 1969),

and this mechanism was suggested in 25% of cases without neck injury (Fleming and Petrie 1968). Downward pressure on the shoulder could produce similar stresses (Garg *et al.* 1968). Obviously the carotid artery is tethered as it enters the skull and less so at its origin from the great vessels at the base of the neck. The details of the exact distribution of the forces involved in stretching have not been well delineated, but one author felt the effect was most significant beyond the origin of the internal carotid artery (Lewin 1968). Also, angulation and tearing could occur where the internal carotid artery enters the skull. In one case, an internal carotid artery was completely transected by a closed injury, with occlusion being caused by external pressure from a haematoma (Jernigan and Gardner 1971).

Several other points should be mentioned. When an atheroma is present in the internal carotid artery, this may be disrupted by trauma and act as a nidus for thrombus formation (Little *et al.* 1969, Ojeman and Moser 1964, Robinson 1961, Toakley and McCaffrey 1965, Yamada *et al.* 1967). On the other hand, in older patients where the carotids have become ectatic, the vessel might be expected to unwind rather than to stretch, which might provide some protection (Little *et al.* 1969). Local anatomical features are also important. The carotid is closely related to the lateral masses of C-1 and C-2 and so may be easily compressed against them by direct injuries or stretched across them in extension and rotation (Boldrey *et al.* 1956, Clarke *et al.* 1955, Fleming and Petrie 1968, Little *et al.* 1969, New and Momose 1969). An abnormal styloid process could also contribute to the mechanism of injury (Eagle 1949). Pharyngeal inflammation may result in adhesions in this region with tethering (BOLDREY *et al.* 1956).

The history and physical examination of the patient may help determine whether local trauma or stretching was the mechanism of injury. Arteriography may also provide some information by locating the site of initial disruption and thrombus formation and thus its relation to other structures. In some cases, occlusion or stenosis has been seen in the upper neck or at the base of the skull (Boldrey *et al.* 1956, Frantzen *et al.* 1961, Friedenbergl *et al.* 1973, Garg *et al.* 1968, Hockaday 1959, Horner *et al.* 1970, Little *et al.* 1969, Mastaglia *et al.* 1971, Miller and Ayers 1967, New and Momose 1969, Ritchie 1961, Schneider 1973, Sullivan *et al.* 1973, Thompson 1963), suggesting that injury occurred at or in the carotid canal or over the upper cervical vertebrae. In one review of traumatic carotid artery occlusions, one-third were more than 3 cm distal to the bifurcation (New and Momose 1969). In another

review, 85% of traumatic internal carotid artery occlusions were noted to be in the cervical carotids, generally 1–3 cm above the bifurcation, while 10% were in the petrous carotid (Zilka 1970). Where stasis is present, special techniques may be needed to demonstrate the exact level of the proximal occlusion (Glickman *et al.* 1972).

Once thrombus formation has begun, two factors are important in determining the ultimate effect of the vascular lesion on the patient's central nervous system. The first is the ultimate extent of the thrombus, and the second is the patient's collateral cerebral blood flow.

The extent of thrombus formation will be determined by the relation between the natural intravascular processes of thrombosis and thrombolysis and will be related to the anatomy of proximal and distal vascular branching with flow factors being important.

At times only stenotic, as opposed to occlusive, lesions may be present (Bickerstaff 1964, Frantzen *et al.* 1961, Friedenberg *et al.* 1973, Garg *et al.* 1968, Gleave 1966, Horner *et al.* 1970, Miller and Ayers 1967, Salmon and Blatt 1968, Schneider *et al.* 1971, Sullivan *et al.* 1975, Yamada *et al.* 1967). Only a few of these stenoses seemed severe enough to be causing symptomatic decreases in cerebral blood flow (Gleave 1966, Horner *et al.* 1970, Salmon and Blatt 1968), and therefore other phenomena may have been at work.

Once a thrombus has occluded the vessel, it will tend to propagate proximally to a bifurcation. Thus, occlusion has been seen commonly at or just above the carotid bifurcation (Sedzimir 1955). It has also been observed that thrombus may extend distally into the middle cerebral or even anterior cerebral artery (Caldwell and Hadden 1948, Caldwell 1936, Fairburn 1957, Murray 1957, Northcroft and Morgan 1944, Sedzimir 1955, Schneider and Lemmen 1952). This has been noted in occlusions due to other causes (Lhermitte *et al.* 1968, Luessenhop 1959). Since it is rare to see the ophthalmic artery fill the siphon, it may be hard to evaluate the distal extent of the thrombus on angiography (Therkelsen and Hornes 1963).

There is then the question of the ultimate fate of the thrombus. Only a few serial arteriograms have been performed in traumatic thrombosis (Frantzen *et al.* 1961, Friedenberg *et al.* 1973, Miller and Ayers 1967, Schneider *et al.* 1971, Sullivan *et al.* 1973, Verbeist and Calliauw 1959). Interesting findings have included development of an occluding lesion from a stenotic lesion (Sullivan *et al.* 1973), proximal propagation of thrombus (Frantzen *et al.* 1961), and also decrease in defects (Frantzen *et al.* 1961, Friedenberg *et al.* 1973, Schneider *et al.* 1971). In one case, there was migration of a thrombus

with eventual resolution (Salmon and Blatt 1968). In another there was complete resolution of an obstructing lesion (Verbiest and Calliauw 1959).

Collateral cerebral vascular anastomoses play an important role in the development of symptoms. Indeed, apparently because of collateral flow, some carotid occlusions may not be symptomatic (Dyken *et al.* 1974, Yashon *et al.* 1964). This has been noted in angiography (Murphey and Maccubbin 1965), or in post-mortem examinations (Fisher 1954) in atheromatous disease, in injuries (Drapanas *et al.* 1970; Monson *et al.* 1969), and in operative situations such as when a carotid has been clamped to protect against aneurysm rupture (Brackett 1953, Luessenhop 1959, Murphey and Maccubbin 1965). In carotid surgery for atheromatous disease, when vessels are often clamped for periods of time during removal of intimal plaques, intravascular pressure measurement and EEG's have predicted adequate collateral circulation (Sundt *et al.* 1974). Internal carotid pressure has also been shown to correlate with cerebral blood flow and eventual toleration of carotid ligation (Fiorani *et al.* 1975, Jawad *et al.* 1975). Also, when symptomatic, carotid occlusion may have a wide range of possible clinical presentations, perhaps indicating the presence of variable collateral patterns. The spectrum of clinical variabilities in carotid occlusion has been discussed in detail, especially in reference to atherosclerotic cerebrovascular disease (Jacobsen and Skinhoj 1957, Johnson and Walker 1951, Webster *et al.* 1950). Also, development of symptoms can only be partly related to time of complete occlusion, since it is known they may not occur immediately after surgical lesions (Luessenhop 1959) or closing of a carotid clamp (Brackett 1953). This may indicate the failure of collateral circulation or may relate to the propagation of thrombus.

The anatomy of normal collateral pathways has been recently reviewed and is fairly well known (Gillilan 1974, Mishkin and Schreiber 1974). The enlargement of collateral vessels in slow occlusions has been extensively studied in the Moyamoya syndrome (Krayenbühl 1975). But, in general, angiographic details and clinical correlations of collateral circulation in acute occlusive disease have not been extensively described. In one series of spontaneous internal carotid artery occlusions it was noted that, if collateral circulation was seen late, this did not necessarily indicate a good outcome. But when seen early, collateral circulation from the posterior communicating artery and contralateral internal carotid artery and to some extent from the ipsilateral ophthalmic artery suggested a favorable prognosis (Jacobsen and Skinhoj 1957). In one post-

traumatic case, progressive development of collateral circulation was shown by serial angiography over an eight month period without coincident clinical improvement (Higazi 1963).

Besides simple thrombosis, injury to a vessel may actually result in a dissection and elevation of an intimal flap and cause a dissecting aneurysm with stenosis, or there may be actual retraction and curling of the flap causing occlusion (Caldwell and Hadden 1948, Dratz and Woodhall 1947, Fletcher *et al.* 1974, Gurdjian *et al.* 1963, Lai *et al.* 1966, Little *et al.* 1969, Murray 1957, New and Momose 1969, Northcroft and Morgan 1944, Ritchie 1961, Sullivan *et al.* 1973). True and false aneurysms have also been seen (Heilbrun and Ratcheson 1972, Margolis *et al.* 1972, Salmon and Blatt 1968, Spencer and Imperato 1969, Teal *et al.* 1972).

It has been suggested that spasm can occur in the internal carotid artery resulting in slowing of flow and turbulence and thus promoting thrombosis (Bland *et al.* 1967, Ecker 1945, Ecker and Riemen-schneider 1953, Suzuki *et al.* 1967, Verbiest and Calliauw 1959). However, the occurrence and significance of spasm in carotid injuries have not been evaluated conclusively. Decreased lumen size may actually only indicate decreased blood flow or perhaps a dissecting aneurysm or thrombus of the vessel wall. Also, when thrombosis occurred, an intimal tear may have been present.

Another cause of symptoms after carotid thrombosis could be emboli arising from the thrombus and blocking intracranial vessels. Emboli have been well described in transient ischaemic attacks and cerebrovascular accidents secondary to extracranial cerebrovascular atheromatous disease with thrombus formation (Ehrenfeld *et al.* 1966, Gunning *et al.* 1964, Wylie and Ehrenfeld 1970). They have also been suggested in connection with post-traumatic carotid thrombosis. Premonitory transient ischaemic attacks have been reported (Fleming and Petrie 1968) and were probably due to emboli. Intracranial occlusions have been described on angiograms with stenotic carotid thrombi, also indicating embolic phenomena (Bickerstaff 1964, Fletcher *et al.* 1974, Frantzen *et al.* 1961, Gleave 1966, Gratzl *et al.* 1975, Lewin 1968, Miller and Ayers 1967, Schneider *et al.* 1971, Sullivan *et al.* 1973). Our patient apparently suffered from this complication, as evidenced by the thrombus in the neck causing partial occlusion and the obstructing lesion at the internal carotid artery bifurcation. Three similar cases have just been reported (Gratzl *et al.* 1975), and in each there was recanalization of the occluded vessel, as in our case. In some reports, emboli were present on arteriography after a post-traumatic thrombus was removed from the internal carotid artery, suggesting that they occurred as the

thrombus was forming (Fleming and Petrie 1968, Houck *et al.* 1964). Emboli have also been seen in post mortem examinations (Gleave 1966, Hughes and Brownell 1968, Loar *et al.* 1973, Towne *et al.* 1972). Early operative intervention may thus be indicated in patients with forming thrombi to avoid embolus formation. Trauma may also cause dislodgement of a fragment of atheroma or an already existing thrombus and secondary embolization (Friedlander 1961, Gurdjian *et al.* 1963).

One might postulate that emboli could arise and cause symptoms and then be resolved without leaving evidence. The resolution of thrombi and emboli has been demonstrated in experimental animals *in vivo* (Honour and Russell 1962). Similarly, when cerebrovascular accidents are studied, intracranial occlusions are most frequently seen early, may be observed to fragment or may disappear on serial angiograms, or may not be seen on late angiograms (Bladin 1964, Bull *et al.* 1960, Dalal *et al.* 1965, Ettinger and Ryan 1967, Gannon and Chait 1962, Heyman 1958, Hollin and Silverstein 1965, Lehrer 1958, Lhermitte *et al.* 1968) suggesting the possibility that clot lysis or recanalization occurred. In certain post-traumatic cases, arteriography some time after hemispheric symptoms occurred showed intimal disruption in the carotid system with open intracranial vessels, suggesting that the symptoms may have been caused by emboli which subsequently dissolved (Fletcher *et al.* 1974, Silvernail *et al.* 1975).

It may be that carotid thrombosis is more frequent in head injuries than we suspect. It might be expected that in many cases a thrombus might be resolved before it occluded the carotid enough to decrease flow and cause symptoms. Also, it is possible that thrombi and emboli could arise and cause neurological deficits and then resolve. If infarction had not occurred, the neurological deficits might clear. This may at times be the origin of symptoms previously attributed to brain contusions.

3. Intracranial Vascular Injuries

The intracranial vascular process in our case might have been an unrelated phenomena. Injury to intracranial vessels can lead to thrombosis, as well as rupture, aneurysm formation, and dissecting aneurysms. Traumatic intracranial vascular occlusions are well described (Glickman 1974, Jacques *et al.* 1975, Lewin 1968). It has been noted that intracranial arteries have a plane of cleavage between the intima and media (Hollin *et al.* 1966, Nedwich *et al.* 1963, Scott *et al.* 1960). Injury would elevate the intima, exposing deeper layers, and this could initiate thrombosis. Indeed, when thrombosed vessels

have been examined at autopsy, initial disruption has usually been found (Bots and Kramer 1964, Dratz and Woodhall 1947, de Veer and Browder 1942, Duman and Stephens 1963, Hassin 1937, Linell and Tom 1959).

Intrinsic fibrinolytic mechanisms can apparently often reopen these vessels. A number of patients have been seen with post-traumatic intracranial occlusions on arteriography, and when followed with serial arteriograms or post-mortem examinations in many (Higazi 1963, Hollin and Silverstein 1965, Hollin *et al.* 1966, Jacobsen and Skinhoj 1957, Verbiest and Calliauw 1959, Wolpert and Schecter 1966), though not all (Duman and Stephens 1963), the vessels were seen to have reopened. Some of these lesions, too, may have been embolic. Similar findings have been seen with spontaneous cerebrovascular accidents, where the most likely time to see an occlusion is as early as possible in the patient's course and where serial angiograms may reveal clearing of vessels (Bull *et al.* 1960, Gannon and Chait 1962, Heyman 1958, Hollin and Silverstein 1965).

In general, patients with intracranial traumatic vascular occlusion have done poorly (Loar *et al.* 1973).

4. Treatment of Traumatic Carotid Thrombosis

Treatment of a disease must be based on two areas of knowledge. First, the natural history of the disease should be determined so it can be decided whether treatment alters it. Second, the purpose and effect of various treatments should be analyzed, and knowledge gained from the treatment of similar diseases should be applied.

The fact of prime importance is that some patients can recover from deficits after a stroke without specific therapy. Presumably, when vessels are occluded and part of the brain is ischaemic and non-functional, the neurons may still survive due to collateral blood flow. Then, with increased collateral flow or with reopening of primary vessels, they can recover function. The complex changes in cerebral blood flow in strokes as related to collateral circulation, hyperaemia, luxury perfusion, loss of autoregulation, the no-reflow phenomenon, and changes in metabolism are now under investigation (Harper *et al.* 1975).

Several studies have indicated that when cerebral blood flow and PO₂ are maintained at even low levels, brain viability may still be preserved for long periods (Denny-Brown and Meyer 1957, Meyer 1958, Schneider 1960). Recent experiments have shown that neurons can survive prolonged ischaemic and hypoxic insults under certain conditions and that changes in the microvasculature play a contributing role to death of nervous tissue (Drewes 1973, Fischer 1973,

Hossman and Kleihues 1973, Kirschner *et al.* 1975, Meyer *et al.* 1972, Meyers 1973, Plum 1973). Though agreement is not universal (Brierley *et al.* 1973, Siesjo and Ljunggren 1973), a number of mechanisms for vascular dysfunction have been suggested, including changes in and around the vessel wall as well as within the vascular lumen (Strock and Majno 1969). This area has been studied extensively in the preservation of organs for transplantation.

These concepts have obvious therapeutic implications. Indeed, hyperosmolar agents have been shown to increase cerebral blood flow after strokes (Fieschi *et al.* 1975). These agents may help reopen microvascular channels by dehydration and shrinkage of vessel walls and their surrounding environs as well as by changing the characteristics of the intravascular contents. Postulating that intravascular clot formation was an important factor, one experimental study using fibrinolytic therapy indicated that pretreatment before circulatory arrest led to better toleration of this insult (Crowell and Smith 1956). Heparin has seemed to have similar effects (Smith *et al.* 1969).

The ability to predict outcome after cerebrovascular occlusion would thus depend on determining collateral blood flow, the speed and extent of any progressive increase in collateral circulation, the speed of reopening of the occluded vascular bed, and the permanent damage from the initial lesion. The propagation of thrombus and the occurrence of emboli could alter the course of the disease, as could permanent changes in the microvasculature.

The natural history of post-traumatic carotid occlusion is, as would be predicted, variable. In one large review, it was noted that most patients fared badly, but that a few did well (Yamada *et al.* 1967). However, in another series, only four of twenty-four patients died, but many had subtotal occlusions (Gleave 1966, Lewin 1968). In one study, cerebral circulation time was examined, and prognosis was best when circulation time was least decreased and when it returned to normal most rapidly (Garg *et al.* 1968).

A number of methods have been used to try to treat post-traumatic carotid occlusions. These have included anticoagulation, interruption of sympathetic input to the cerebral vascular system, either by stellate ganglion block or surgical sympathectomy, and ligation of the clotted vessel above and below the occlusion to prevent thrombus propagation and embolism. These therapeutic techniques have not been studied systematically. They were used in single cases or small series without controls, and therefore statistical evidence as to their effectiveness could not be obtained. In general, they are not well accepted today (Lewin 1968).

In a definitive review of stellate ganglion block in spontaneous cerebrovascular occlusions, no beneficial effects were noted (Millikan *et al.* 1961). The relationship of sympathetic influence to cerebral blood flow is, however, still being studied in physiological (Fitch and MacKenzie 1975, Gotoh *et al.* 1975, Kovach *et al.* 1975, Sercombe *et al.* 1975) and anatomical experiments (Sato and Suzuki 1975), and perhaps alteration of sympathetic tone may some day be shown to be helpful in cerebrovascular disease.

Other treatments which have been suggested include hyperbaric oxygen (Illingworth 1962) and hypertension, but it is not clear that these have been attempted.

Early experience with direct operative intervention was variable but, in general, not overwhelmingly encouraging. Until 1967, operated patients seemed to do better than those not operated on (Yamada *et al.* 1967). Since that time, a number of surgeons have noted encouraging results (Garrison *et al.* 1975, Little *et al.* 1969, Therkelsen and Hornes 1963, Zilka 1970) while others had an opposite experience (Berman 1975, Horner *et al.* 1970, Hughes and Brownell 1968, Jernigan and Gardner 1971, Lewin 1968, Olafson and Christoferson 1970). Patients with stenotic lesions especially have done well with surgery (Fletcher *et al.* 1974, Yamada *et al.* 1967). One author has suggested that better results would be expected in young patients. Because, in the elderly, intracranial arteriosclerosis may add in a variety of ways to the impact of the initial ischaemia (Therkelsen and Hornes 1963).

It is fairly easy technically to open occluded vessels after they have been thrombosed for up to 48 hours (DeBakey *et al.* 1962, Murphey and Maccubbin 1965) or with special techniques, after longer periods (Blaisdell *et al.* 1969, Blaisdell *et al.* 1966, Cohen *et al.* 1968). A Fogarty catheter technique may be used to extract thrombi from the distal internal carotid artery (Garamella *et al.* 1966).

But it is well known that patients with spontaneous carotid occlusions operated on early do not do well, or may do even worse, than those who are not operated on (Blaisdell *et al.* 1969, Murphey and Maccubbin 1965). One series was more encouraging about the results of early surgery in patients with spontaneous occlusions with deficits (DeBakey *et al.* 1962). The problem is that when a compromised vascular bed is reopened, an ischaemic infarct may be converted into a haemorrhagic infarct. This has been seen to occur in spontaneous cerebrovascular occlusion (Blaisdell *et al.* 1969, Bruetman *et al.* 1963, Rob 1969, Wylie *et al.* 1964) and has also happened in a case of post-traumatic thrombosis (Towne *et al.* 1972). On the other hand, it has been shown that a carotid artery occluded after trauma can open

spontaneously without disaster (Verbiest and Calliauw 1959), as is true for other types of vascular occlusions (*vide supra*). Serial brain scans have been used to try to evaluate the blood-brain barrier and thus the state of the vascular bed in order to time arterial reconstruction (Cohen *et al.* 1968). Current feeling is that positive scans may correlate with new capillary growth, not injured vessels or secondary oedema (Verhas *et al.* 1975), so the test may not be too helpful.

Two newer therapeutic approaches for cerebrovascular occlusive disease must be mentioned, extracranial-intracranial microvascular anastomosis and thrombolysis.

Because of the operating microscope and the development of fine instruments and sutures, it is now possible successfully to anastomose scalp vessels to cortical vessels. A recent report describes the use of this technique in one patient with post-traumatic carotid thrombosis and two patients with stenotic carotid lesions with apparent intracranial emboli (Gratzl *et al.* 1975). Post-operative angiography and cerebral blood flow studies gave evidence that the anastomoses were functioning, and it is possible that some improvement in neurological function in two patients may have been due to increased blood flow.

Thrombolytic drugs provide another therapeutic possibility which can be considered for use in thrombotic or embolic vascular occlusions.

Two thrombolytic agents, streptokinase and urokinase, have generally been accepted as being effective (Fletcher 1969, Sherry 1968). They are both plasminogen activators. Both agents are selectively attracted to gel plasminogen in a thrombus. Streptokinase is a bacterial endotoxin which acts by combining with and altering the configuration of plasminogen leading to its activation. Because streptococcal infections are common, streptokinase antibodies are ubiquitous and a high loading dose is usually used, followed by a smaller maintenance dose given for a variable period of time. Urokinase is a proteolytic enzyme found in human urine. Urokinase causes less side effects than streptokinase, but it has not been approved for general use and is only available as a research drug. Both agents are effective in thromboembolic disease, as shown recently in a study on human pulmonary emboli (Bell 1975). When these agents are used, laboratory tests can provide evidence of thrombolytic activity, but the changes do not correlate well with clinical effectiveness. It is also difficult to determine the risk of haemorrhagic complications. There is still work needed to determine optimal dosage schedules, and the use of segmental as opposed to systemic infusion must be investigated more fully.

There was some work in the early 1960's dealing with Thrombo-

lysin therapy in cerebrovascular occlusions in animals and in man. Thrombolytic is advertised as exhibiting profibrinolytic-activator and fibrinolytic properties and is prepared by activating a human blood plasma fraction with streptokinase. It has been suggested that streptokinase was the effective thrombolytic agent (Fletcher *et al.* 1961) and that there was need for standardization of the drug (Fletcher *et al.* 1962). Early work indicated that Thrombolytic promoted clot dissolution and was fairly well tolerated. However, the largest trial of this drug in human cerebrovascular disease was fairly small and left many unanswered questions, as indeed the authors pointed out (Herndon *et al.* 1961, Meyer *et al.* 1963, Meyer *et al.* 1962).

As for other modalities, the problems included selection of appropriate patients, evaluation of effectiveness of therapy, and risks of turning ischaemic infarcts into haemorrhagic infarcts. One report of a trial of streptokinase indicated that this could occur (Meyer 1964). Cerebral blood flow monitoring may provide the answers to these problems, for if residual collateral flow is sufficient, it might be expected that the brain is still viable and also that it would tolerate reopening of the vascular bed. Indeed, it has been suggested that the use of thrombolytic therapy in cerebrovascular disease should be reconsidered (Sherry 1968), and guidelines for thorough, systematic protocols have been outlined (Fletcher 1969).

Although the use of thrombolytic therapy for post-traumatic carotid thrombosis has been suggested in the past (Houck *et al.* 1964), as far as we know this is the first time it has actually been reported. It may very well have been that our patient's gratifying clinical and angiographic recovery was fortuitous, since we do not know if we really accelerated thrombolysis. It might have been of advantage to deliver the drug by segmented infusion when our angiographic catheter was in place.

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