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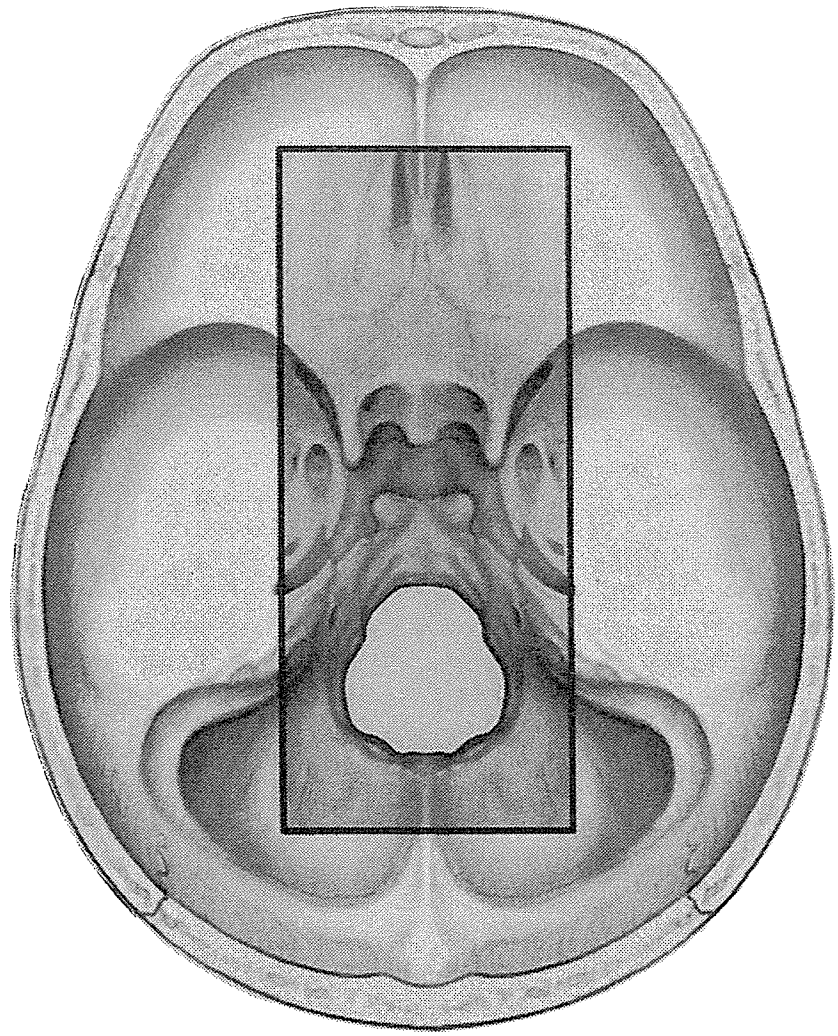

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Hemichorea due to hemodynamic ischemia associated with extracranial carotid artery stenosis

Report of two cases

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In this paper the authors describe two patients with recurrent hemiparesis and limb shaking that gradually progressed to hemichorea. Cerebral angiography confirmed severe unilateral internal carotid artery stenosis (95%) contralateral to the hemichorea. The cerebral blood flow, assessed using *N*-isopropyl-p-(iodine-123) iodoamphetamine single-photon emission computed tomography (SPECT), disclosed markedly decreased vascular reserves in both patients. After carotid endarterectomy was performed, the hemichorea gradually subsided and SPECT confirmed increased cerebral perfusion. The results in these cases indicate that surgical revascularization is effective for hemichorea due to cerebral ischemia with reduced vascular reserve.

KEY WORDS • **carotid endarterectomy** • **carotid artery stenosis** • **hemichorea** • **cerebral blood flow**

INVOLUNTARY limb shaking is an unusual manifestation of transient ischemic attacks associated with carotid artery occlusive disease; it usually lasts up to 60 seconds.[1–3,5–7,9,11,18,20,21,23,26,27,29,30,32–34] In patients with HCHB, another uncommon movement disorder, the involuntary movements are usually continuous and last for weeks or months.[4,18,19] Lesions in the contralateral caudate nucleus, putamen, thalamus, subthalamus, pons, midbrain, or subcortical white matter are thought to be responsible for such movement disorders.[19] In HCHB, the lesion can be located anywhere in the cortico-striato-pallido-thalamo-cortical feedback loop.[8,11] Hemichorea–hemiballism associated with carotid artery occlusive disease is extremely rare: its origin and surgical treatment remain controversial because there is not enough knowledge regarding the cerebral hemodynamic insufficiency in these patients.

In this report we evaluate the CBF in two patients suffering from hemichorea and severe extracranial carotid artery stenosis by using ^{123}I-IMP SPECT, and we discuss the efficacy of surgical treatment. This is the first at-rest, acetazolamide-enhanced SPECT study performed before and after CEA to assess the contribution of hemodynamic factors to the development of hemichorea associated with severe ICA stenosis.

Abbreviations used in this paper: CBF = cerebral blood flow; CEA = carotid endarterectomy; ECA = external carotid artery; HCHB = hemichorea–hemiballism; ICA = internal carotid artery; ^{123}I-IMP = *N*-isopropyl-p-(iodine-123) iodoamphetamine; MR = magnetic resonance; SPECT = single-photon emission computed tomography.

Case Reports

Case 1

History. This 75-year-old right-handed man with hypertension, hypercholesterolemia, and a 50-year history of smoking suddenly experienced recurrent transient left hemiparesis. The episodes, which occurred once or twice a week, involved only his left arm and lasted a few seconds. There were no provocative factors. He had no history of convulsive disease, orthostatic hypotension, diabetes mellitus, or parkinsonism. Involuntary continuous trembling of his left arm appeared 1 month after the onset of his first transient ischemic attack; it disappeared during sleep and could be voluntarily suppressed for only a short time. He was admitted to our hospital for further examination.

Examination. On admission, the patient was alert. There was very mild upper hemiparesis of his left arm and mild bilateral dysfunction of vibration sensation. There were no carotid artery bruits. In the pronated and supinated positions, the distal portion of his left arm twitched or jerked rapidly; the distal portion of his leg on the same side also shook. His gait was slightly disturbed because of clumsy choreiform left leg movements. The involuntary movements were diagnosed as hemichorea by a neurologist. There was no involuntary movement of the facial muscles.

Axial T_2-weighted MR images revealed small areas of hyperintensity in the bilateral corona radiata (Fig. 1). A right carotid artery angiogram demonstrated severe stenosis (95%) of the right ICA (Fig. 2A) and slow filling of the intracranial arteries (Fig. 2B and C). At-rest ^{123}I-IMP SPECT showed severe hypoperfusion within the right hemisphere (Fig. 3A and D). After acetazolamide was administered, SPECT studies were obtained that revealed a marked decrease in the vascular reserve capacity in the right hemisphere including the basal ganglia (Fig. 3B and E).

Operation and Postoperative Course. After a right CEA had been performed, we obtained SPECT studies, which demonstrated improvement in the CBF in the right hemisphere including the basal ganglia (Fig. 3C and F). At 3 months post-CEA, the hemichorea in the patient's left upper and lower limbs had ceased at rest; it disappeared completely by 2 years.

Case 2

History. This 77-year-old woman was admitted to our hospital for evaluation of ICA stenosis demonstrated on MR angiography performed elsewhere. Her history was notable for hypertension, noninsulin-dependent diabetes mellitus, chronic occlusive pulmonary disease, and hypercholesterolemia, but not for convulsive disease, orthostatic hypotension, or parkinsonism.

Examination. On admission the patient was alert and without neurological deficits except that her left leg shook intermittently for a few minutes at a time. The involuntary limb movement was transient, brief, and occurred several times a day; during the attacks, the distal portion of her left leg pronated and supinated for approximately 2 or 3 minutes and then the shaking stopped. There were no provocative factors. Over the course of the next 3 months the involuntary left limb shaking progressed to hemichorea when she was awake.

Areas of hyperintensity in the head of the caudate nucleus on the right side, bilateral basal ganglia, and centrum semiovale were demonstrated on T_2-weighted MR images (Fig. 4). A right carotid artery angiogram showed severe stenosis (95%) of the right ICA (Fig. 5A) and slow filling of the intracranial arteries on the same side (Fig. 5B and C). At-rest SPECT disclosed severe hypoperfusion within the right hemisphere including the basal ganglia (Fig. 6A and D). After acetazolamide was administered, SPECT studies demonstrated a marked decrease in vascular reserve capacity in the right hemisphere including the basal ganglia (Fig. 6B and E).

Operation and Postoperative Course. The patient underwent CEA 3 months after the deterioration of her symptoms; subsequently, her hemichorea slowly subsided. Postoperative SPECT demonstrated improved CBF in the right hemisphere including the basal ganglia (Fig. 6C and F). Her hemichorea gradually improved and is apparent only in her gait 18 months after CEA.

Discussion

We describe two patients whose hemichorea due to a decrease in CBF and vascular reserves in the contralateral hemisphere was associated with ICA stenosis. Because the involuntary movements occurred subsequent to recurrent hemiparesis or intermittent limb shaking, we suspected hemodynamic factors. Our results suggest that hemichorea occurs during the development of hemispheric hypoperfusion and that revascularization may alleviate this symptom.

Our search of the literature found only three earlier reports of HCHB associated with major extracranial atheromatous ICA stenosis.[8,23,25] In two patients, HCHB showed marked improvement after CEA.[23,25] In another patient, the hemichorea gradually subsided naturally; however, there was an incremental worsening of hemiparesis.[8] The patient in our Case 1 experienced recurrent transient hemiparesis that progressed to hemichorea, suggesting that increasing involvement of the premotor cortex or corticostriatal fibers resulted in hemichorea. Although an association between moyamoya disease and hemichorea has been reported,[10,11,22,24,28,31] only a few patients described underwent surgical reconstruction.[10,11,22,31] After these patients had undergone an ECA–ICA bypass, their hemichorea subsided or disappeared slowly as their CBF normalized. These results suggest that impaired CBF may be an important contributing

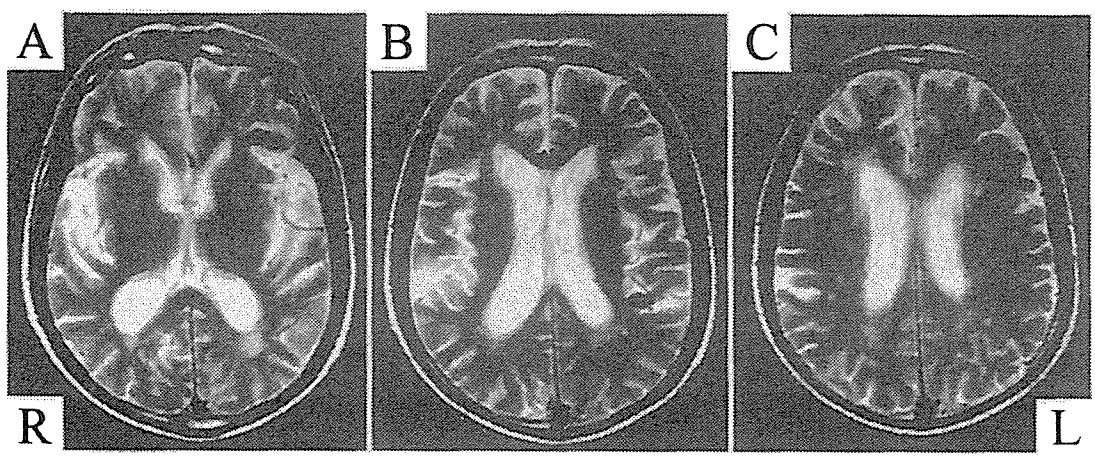

FIG. 1. Case 1. Axial T_2-weighted MR images obtained at admission, showing small areas of high signal intensity in the bilateral corona radiata. L = left; R = right.

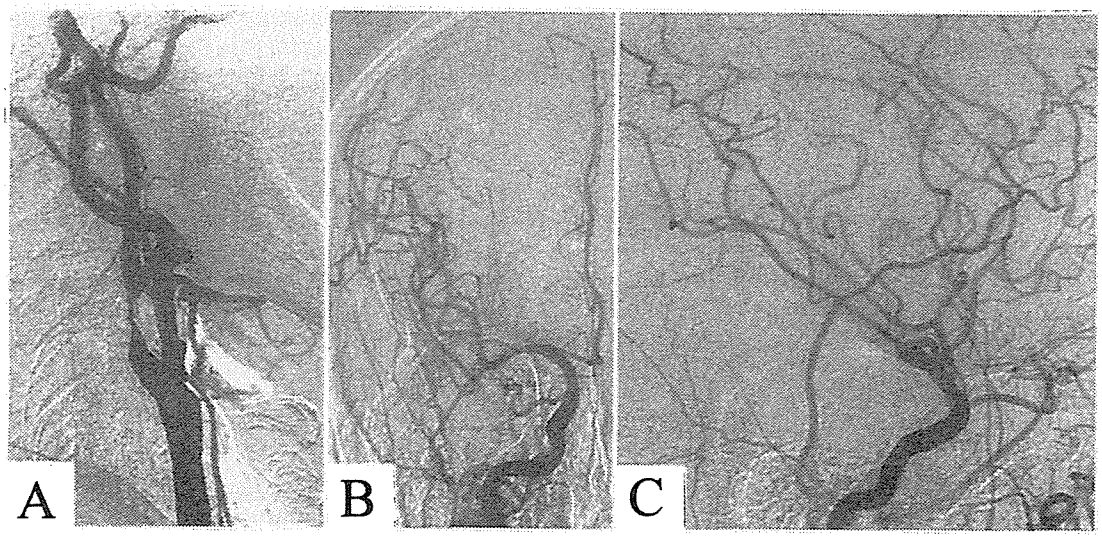

FIG. 2. Case 1. A: Right carotid artery angiogram showing severe stenosis of the ICA. B and C: Right carotid artery angiograms demonstrating delayed blood flow to the intracranial circulation (A and C, lateral views; B, anteroposterior view).

factor in hemichorea associated with intracranial ICA stenosis.

It has been reported that HCHB may occur in patients whose areas of ischemia are located within the cortico-striato-pallido-thalamo-cortical feedback loop.[8,11] The infarct sites, where CBF is thought to be most severely impaired, and the region of the perfusion defect and decreased reserves must be considered, because the reversible involun-

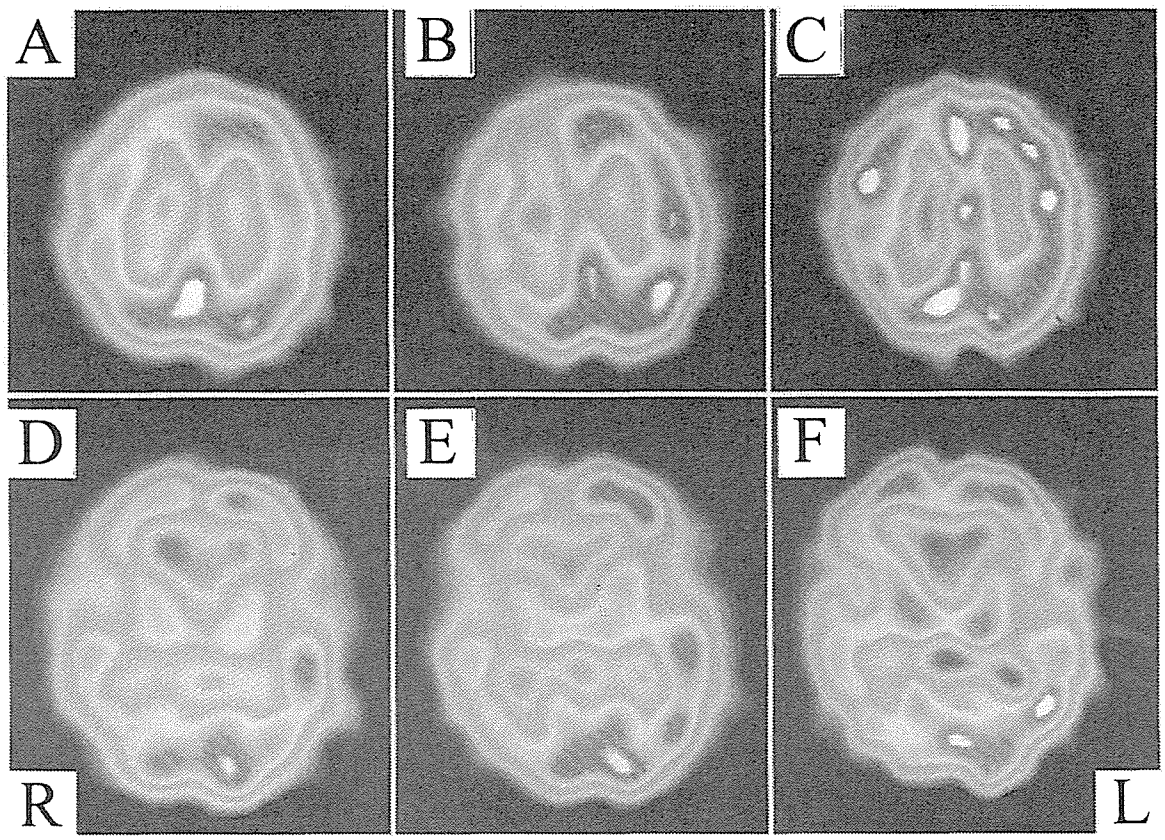

FIG. 3. Case 1. A and D: Preoperative ^{123}I-IMP SPECT scans demonstrating severe hypoperfusion in the right hemisphere including the basal ganglia. B and E: Preoperative ^{123}I-IMP SPECT scans obtained after acetazolamide infusion, showing a marked decrease in the vascular reserve in the right hemisphere including the basal ganglia. C and F: Postoperative ^{123}I-IMP SPECT scans demonstrating improvement in the CBF in the right hemisphere including the basal ganglia.

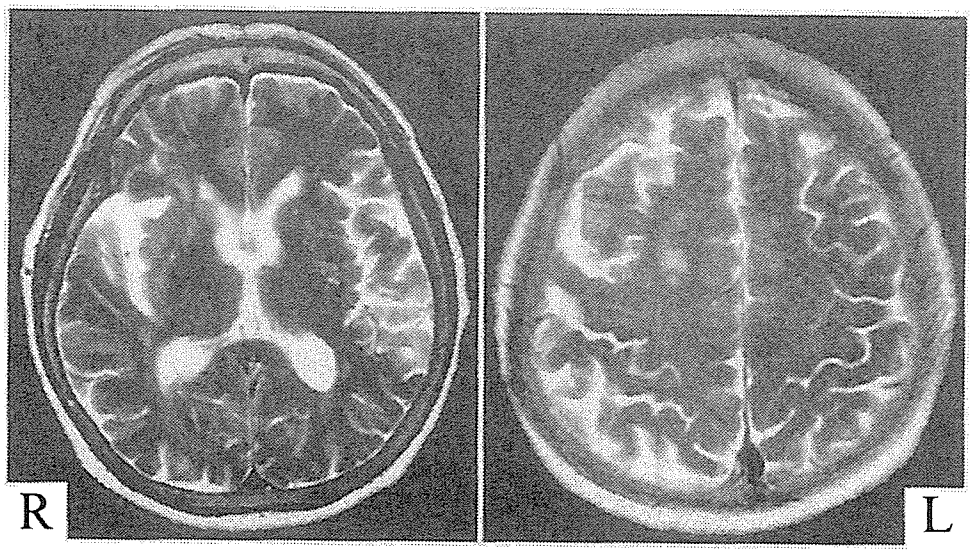

FIG. 4. Case 2. Axial T_2-weighted MR images obtained at admission, showing small areas of high signal intensity in the right white matter in the frontal lobe and bilateral basal ganglia.

tary movements differed in earlier reports in patients with HCHB associated with carotid occlusive disease. Many infarcts occur in the frontal subcortical white matter[8,10,11,25,27] and basal ganglia infarcts are relatively rare.[10,23,25] Although in earlier reports the area of decreased CBF varied from the cortex to the basal ganglia,[8,10,11,25] the region of decreased vascular reserves involved the frontal lobe in two of three cases.[10,11] This suggests that lesions on the anterior border zone are associated with the greatest consequence. The infarcts in our patients were located in the deep anterior watershed (Case 1) and the frontal centrum semiovale and basal ganglia (Case 2), regions considered to lie within the anterior watershed area. The regions of decreased perfusion and autoregulatory reserve were hemispheric. Our results support the hypothesis that connecting fibers in the superficial or deep anterior watershed were exposed to ischemic conditions and that the selective disruption of corticostriatal projections from the indirect pathway resulted in the hemichorea observed in our patients.

Conservative medical therapies have been attempted in patients with limb shaking. Administration of antiplatelet agents and lowering the dose or discontinuing administration of antihypertension agents have resulted in marked improvement in some cases.[1,2,16,23,30] Anticonvulsion agents and levodopa have been ineffective in most patients.[1,2,12,32,34] The most common and effective treatments are surgical revascularization, for example, CEA,[1,2,14,20,29,32,33] CEA specific to the ECA,[14,33,34] and ECA–ICA bypass surgery.[1,5,7,9,11,13,32,33] In

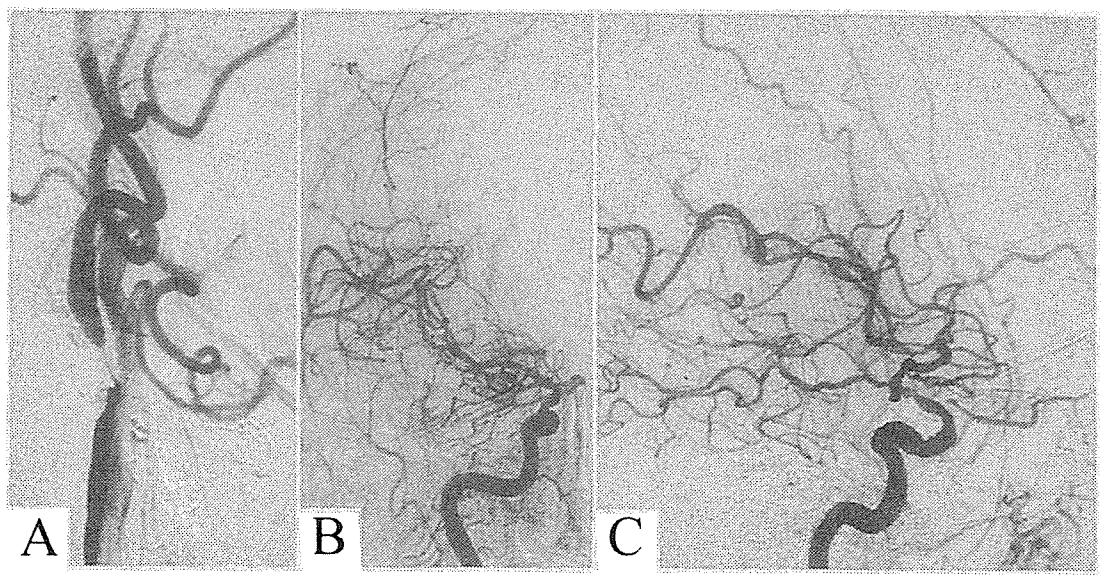

FIG. 5. Case 2. A: Right carotid aftery angiogram demonstrating severe carotid artery stenosis. B and C: Right carotid artery angiograms showing stenosis of the ICA at the supraclinoid portion and slow filling of the intracranial middle cerebral artery (A and C, lateral views; B, anteroposterior view).

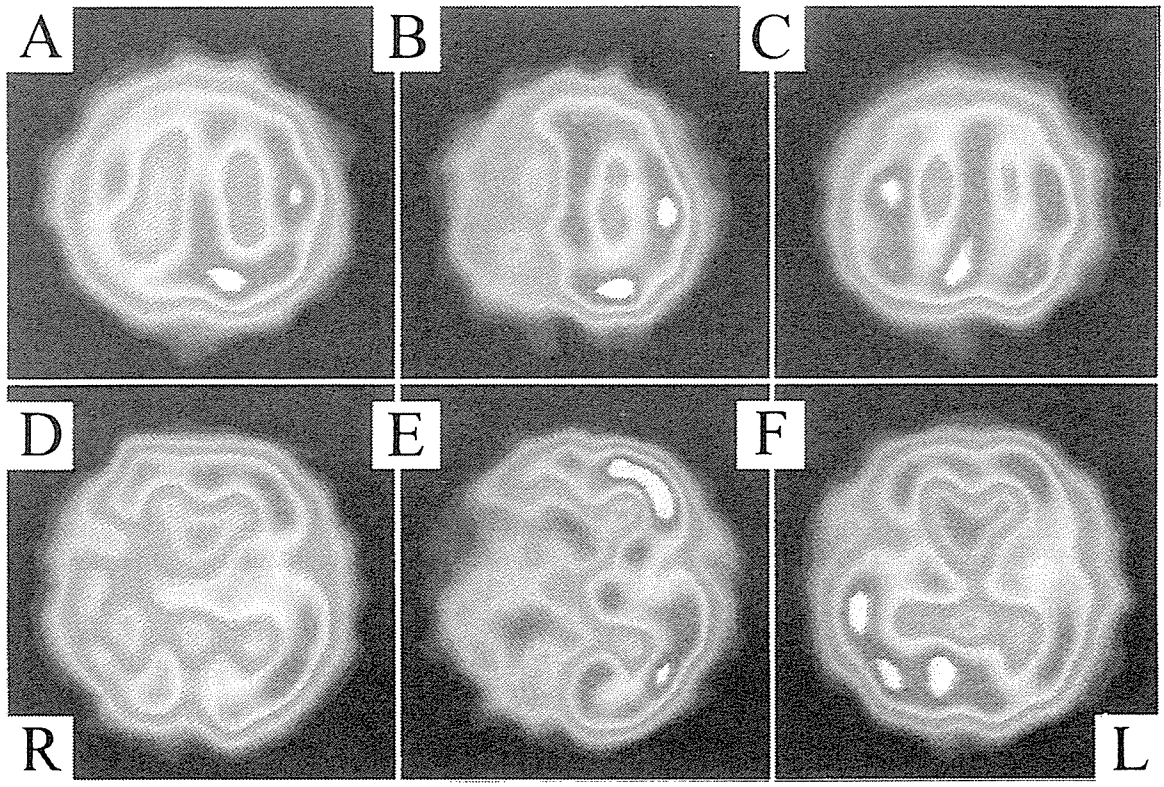

FIG. 6. Case 2. A and D: Preoperative ^{123}I-IMP SPECT scans showing severe hypoperfusion in the right hemisphere including the basal ganglia. B and E: Preoperative ^{123}I-IMP SPECT scans obtained after acetazolamide infusion, revealing a marked decrease in vascular reserve in the right hemisphere including the basal ganglia. C and F: Postoperative ^{123}I-IMP SPECT scans demonstrating improved CBF in the right hemisphere including the basal ganglia.

some patients with spontaneous collateral compensation, a natural cure is obtained, whereas in others the condition may progress to hemichorea. Although in many patients infarct lesions appeared in the frontal white matter,[1,2,7,11,30,33,34] in others there were no lesions.[1,2,14,29,32,33] The region involved in the perfusion defect frequently includes the frontoparietal lobes,[6,7,11,12,29,30,34] and decreased vascular reserves are often hemispheric.[2,5,7,12,14] There is some evidence for a correlation between limb shaking and ischemia in the anterior border zone. We suggest that decreased vascular reserves constitute a risk factor for the progression of limb shaking to HCHB. In addition we stress that before undertaking any revascularization procedures, the status of a patient's cerebrovascular reserves must be determined.

We propose that the mechanism underlying the development of hemichorea associated with carotid artery occlusive disease is strongly correlated with ischemia in the anterior border zone and that surgical revascularization is an effective therapy in these patients. Cytotoxic edema appears to be an unlikely candidate for the cause of treatable involuntary movements in our Case 2 because the patient's leg shaking continued for 3 months and gradually worsened in the absence of further infarctions.

Conclusions

We describe two patients with severe hemodynamic ischemia due to severe carotid artery stenosis who manifested hemichorea. Carotid endarterectomy effectively improved this rare disorder and normalized the CBF.

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23. バイパス手術の適応と手術成績

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はじめに

1985年の国際共同研究でアテローム血栓性脳主幹動脈閉塞性病変に対するEC-IC bypass術の有効性が認められなかったことより[4]，欧米ではこの手術はほとんど施行されなくなった．しかし，その研究では脳血流検査が必須ではなく，十分な評価がなされていなかった[1]．平成10年より本邦で施行されたJET studyでは定量的脳血流検査を必須とし，かつ重度の脳血流低下を示した症例のみを対象としてstudyを行ったところ[3]，薬物治療群より有意にbypass手術群が脳梗塞再発を防いだという結果が得られた．しかしJET studyで示された適応基準に従って手術症例を選べば，当科においても手術症例は減少している．

もやもや病に対して虚血症例では以前よりEC-IC bypass術が施行されてきたが，成人の出血例に対するEC-IC bypass術の効果については現在JAM trailで研究中である[2]．また動脈瘤手術時のbypassの適応も明らかではない．以上のような環境下で，限られた症例に対するEC-IC bypass術の成績を検討したので報告する．

対象と方法

1997年1月から2005年5月までに当科で施行したEC-IC bypass手術例83例を対象とした．そのうちアテローム血栓性脳梗塞に対するbypassは58例でSTA-MCA bypass 56例(JET登録9例を含む)，STA-SCA 2例であった．もやもや病に対してEC-IC bypass術を19例(JAM登録1例を含む)施行した．また脳動脈瘤5例に対してhigh flow bypass 2例，STA-MCA 1例，STA-SCA 1例，OA-PICA 1例，その他1例を施行した．

1. 手術適応

① アテローム血栓性脳梗塞

原則としてJETの登録基準を遵守した[3]．すなわち症候性主幹動脈狭窄・閉塞を有する症例で，術前のRankin Scale(RS)が1-2である症例でかつ^{123}I-IMP SPECTで安静時脳血流が正常(40 ml/100 g/min)より20%以上低下し，かつacetazolamide負荷による血管反応性が10%未満の増加にとどまる症例を手術適応ありとした．

② もやもや病

非出血例では症候性側でかつRS 1-3までの症例で，脳血流が低下している例はもちろん，軽度の血流低下例でも直接吻合を主とする血行再建術を施行してきた．

また成人出血例ではJAM trialの適応を遵守している．すなわち年齢が65歳までででかつ，RSが1-3までの症例とした．

③ 脳動脈瘤に対するバイパス術

脳動脈瘤のtrappingやocclusionを行う際の血流確保の手術としてEC/ICバイパスを行った．その適応は術前のバルーンマタス試験で陽性の症例，術中閉塞試験で陽性の症例でかつ65歳以下の症例とした．

2. 手術手技

① STA-MCA bypass

全身麻酔下で浅側頭動脈頭頂枝の直上を皮膚切開し，頭頂枝を剝離する．側等筋をY-shapedに切開して，5×5 cmの骨窓を置く．硬膜を切開し

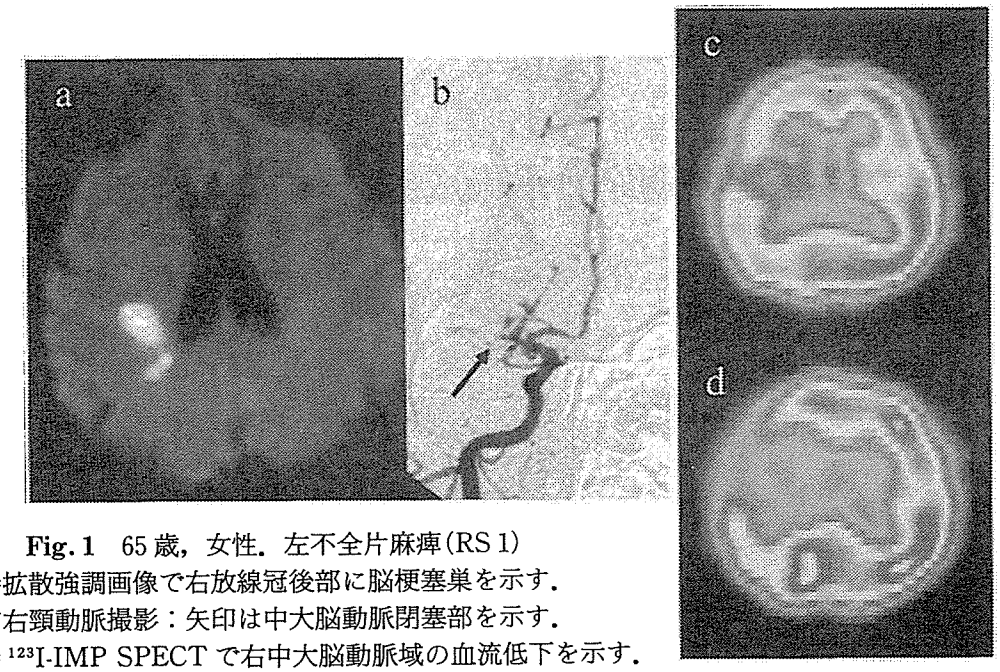

Fig. 1 65歳，女性．左不全片麻痺(RS 1)
a：発症時拡散強調画像で右放線冠後部に脳梗塞巣を示す．
b：手術前右頸動脈撮影：矢印は中大脳動脈閉塞部を示す．
c：安静時 ^{123}I-IMP SPECT で右中大脳動脈域の血流低下を示す．
d：Acetazolamide 負荷 ^{123}I-IMP SPECT で右中大脳動脈域の血管反応性低下を示す．

て，脳表の中大脳動脈皮質枝に浅側頭動脈を吻合した．

② もやもや病に対する STA-MCA bypass＋EDAS（浅側頭動脈前頭枝）

上記の手術手技に加えて，前頭枝を毛髪生え際から約 5 cm 剝離し，直下に 3×3 cm の骨窓を作成する．硬膜を X-shaped に切開し，前頭枝を含んだ gareal flap を硬膜に縫合する EDAS を追加した．

③ 脳動脈瘤 trapping 術に対する high flow bypass

Radial artery を 15-16 cm 採取し，この血管を使用して外頸動脈起始部と中大脳動脈 M2 部に high flow bypass を置いた(上山方式)．

結　果

術中全例で patency を確認した．3 例(3.6%)で major complication が生じ，8 例(9.6%)で一過性の合併症を呈した．

① アテローム血栓性脳梗塞

術中測定した STA の flow volume の平均は 28.8 ml/min で，STA diameter の平均は 1.4 mm，MCA diameter の平均は 1.3 mm，中大脳動脈閉塞時間は平均 42 min であった．合併症として major complication を 2/58(3.7%)認めた．1 例は反対側に硬膜下血腫を認め開頭血腫除去術を施行した(現在 RS 1)．もう 1 例は脳幹・小脳梗塞に対して STA-SCA bypass を施行し，術後側頭葉に脳浮腫を認め，軽度の片麻痺を呈し，RS 3 で退院した．また術後放線冠に小さなラクナを手術側に認めた minor complication を 1 例(1.7%)認めたが RS 1 で退院した．経過 follow-up 中に手術を要する慢性硬膜下血腫を 2/58(3.7%)に認めた．最終 follow-up 時の RS は 1 が 73.3%，2 が 12.5%，3 が 14.2% であった．

代表例を **Fig. 1, 2** に示す．

② もやもや病

術中測定した STA flow volume の平均は 16.8 ml/min，STA diameter の平均は 1.1 mm，MCA diameter の平均は 1.1 mm，中大脳動脈の閉塞時間は平均 41 min であった．このうち術後硬膜下出血をきたして死亡した major complication が 1/19(5.3%)で生じ，minor complication が 3/19(15.8%)で生じたがその内訳は skin complication が 2 例，hyperperfusion による失語の一過性の増悪が 1 例に認められた．

③ 脳動脈瘤に対する bypass

5 症例では術中術後に神経学的増悪は認められ

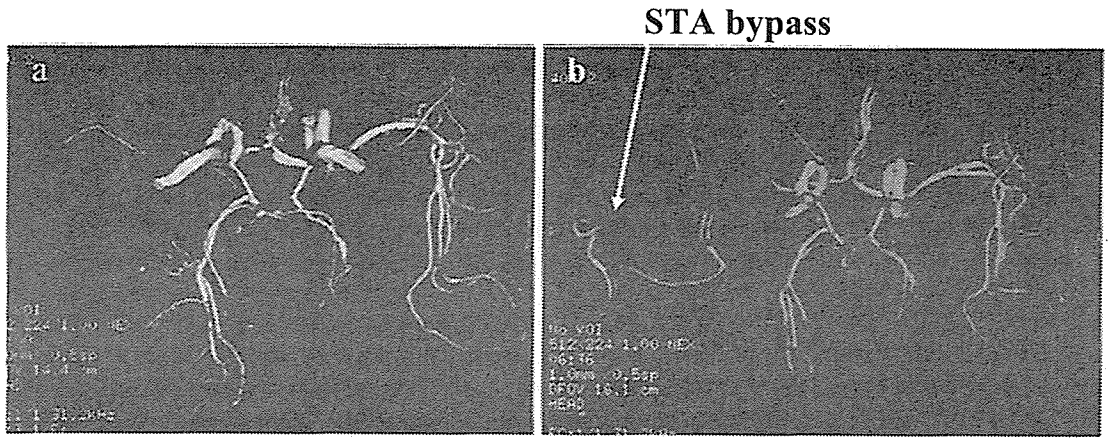

Fig. 2　65歳，女性．左不全片麻痺(RS 1)術前・術後 MRA
a：3T-MRI による術前の MRA(volume rendering 表示)で右中大脳動脈閉塞を示す．
b：術後 MRA で浅側頭動脈から中大脳動脈が良好に描出されている(矢印)．

なかった，経過中5症例とも破裂，再破裂はなかった．また動脈瘤の拡大例もなく，動脈瘤の消失例が2例に認められた．最終追跡時の RS は1が4例，RS 3が1例であった．

考　　察

1985年に結果がでた EC/IC bypass 術の国際共同研究では，手術初期の合併症発生率が高く，薬物治療に対して効果がなかった[4]．今回のわれわれの検討ではアテローム血栓性脳梗塞に対する EC/IC bypass 後の合併症率は3.7%であった．JET での手術合併症率は0%であり，非常に成績はよいが，すべての手術で0%とはいかないまでも，薬物治療群に対して有意な効果を出すためには合併症を極力低くしなければならない．JET 参加施設の登録前に行った各施設の EC/IC bypass の mortality & morbidity rate の平均は2.7%であった．ゆえにこのレベルに手術成績を維持できる施設で手術を行えば JET study の結果のように薬物治療群に比較して有意差が出ると考えられる．手術の注意点として最も重要なことは JET の登録基準を満たす症例のみを手術適応とすることは第1であるが，その他として，術前，術後の血圧管理，脱水の予防など全身管理が重要であろう．また適応を絞れば手術件数が当然少なくなり，術者の技術をどう維持するかが重要である．特にもやもや病に対するバイパス術はアテローム血栓性脳梗塞に対するものより，技術的にはさらに難しくなる．細い血管でも直接バイパスができればその日から症状の改善も得られることが多く，安易に間接バイパスに終わらせることは慎むべきと考える．また成人の出血発症に対するバイパス術に対しては JAM trail の結果が待たれるところである．

脳動脈瘤に対するバイパスの手術適応は一定の見解はなく，かつ high flow bypass を行う機会は非常に少ない．技術的維持はさらに難しく，このような症例はやはり1施設にできるだけ集めて症例を多くこなすシステムを確立すべきであろう．

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Penetrating Atheroma in Cervical Carotid Artery Stenosis

—Case Report—

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Abstract

A 61-year-old male presented with left hand motor weakness associated with cerebral infarction in the right frontal lobe. Right common carotid angiography demonstrated a 66% stenosis and carotid duplex scan demonstrated intermediate echogenic plaque, indicating typical carotid plaque. Carotid endarterectomy was performed 22 weeks after the ischemic onset. During exposure of the carotid artery, a soft and yellowish mass (5 × 5 mm) was observed in the lateral wall of the carotid bulbus, which was not covered with adventitia but with thin connective tissue. The mass was removed en-bloc with a small part of the surrounding arterial wall combined with ordinary endarterectomy. The artery was closed with a collagen-impregnated polyester patch graft (Hemashield patch™) to maintain adequate arterial lumen. Histological examination of the removed plaque confirmed that atheroma had protruded from the intima through the media as well as the adventitia and formed an extra-arterial mass. Such a case requires great care to dissect the carotid artery to prevent premature disintegration of the atheroma.

Key words: atherosclerosis, carotid endarterectomy, penetrating atheroma, plaque

Introduction

Cervical carotid artery stenosis resulting from atherosclerotic changes is one of the major causes of stroke, and accounts for 16–33% of all cases of ischemic stroke.[3,8] Atherosclerosis is usually characterized by the formation of intimal lesions called atheroma that protrude into and obstruct the vascular lumen. Atherosclerotic plaque originates in intimal injury.[9] Foam cells penetrate the injured wall and cholesterol accumulates. Atheromatous plaque is limited to the intima at first, and the media becomes weakened with the progression of atherosclerosis. The media is often involved but adventitial involvement is rare. When carotid endarterectomy (CEA) is indicated, one of the most important technical concerns is to dissect the intimal plaque but preserve the media and the adventitia as far as possible. If the media as well as the adventitia are invaded by the plaque, then special attention is needed not to injure the adventitia.

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Here, we present a rare case of cervical internal carotid artery (ICA) stenosis caused by atheromatous plaque which penetrated the adventitia and formed a mass outside the artery. CEA required meticulous dissection and closure of the artery.

Case Report

A 61-year-old man presented with left hand motor weakness and was admitted to a neighboring hospital on the next day. T_2-weighted magnetic resonance imaging on admission showed a small hyperintense area in the right precentral gyrus (Fig. 1A). Conventional angiography showed a 66% right cervical ICA stenosis by the North American Symptomatic Carotid Endarterectomy Trial method (Fig. 1B). He was treated with heparin and then ticlopidine, then transferred to our hospital 40 days after the onset for possible surgical treatment.

On admission he presented with residual mild left hand motor weakness. He had a medical history of hypertension and hyperlipidemia. Carotid duplex study showed that the intima-media thickness was 4.9 mm in the right carotid bulbus. The echogenicity

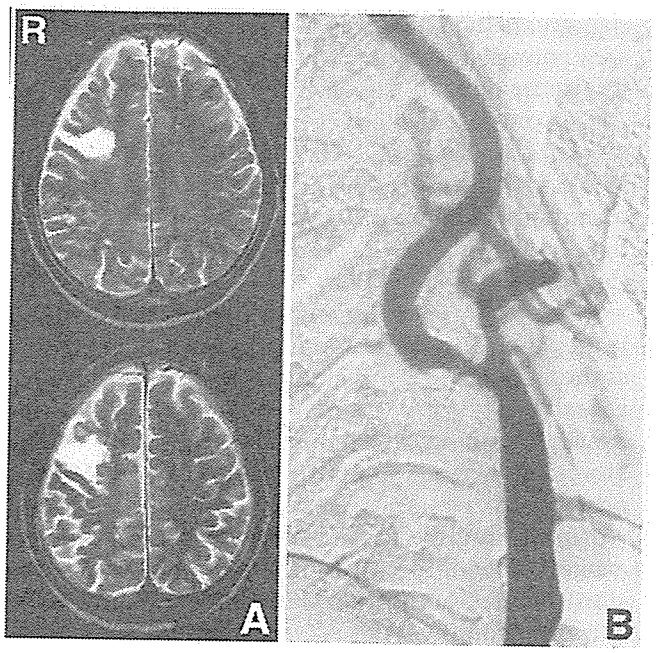

Fig. 1 **A: Preoperative T_2-weighted magnetic resonance images showing a small hyperintense area in the right precentral gyrus. B: Right common carotid angiogram showing a stenosis of 66% by the North American Symptomatic Carotid Endarterectomy Trial method.**

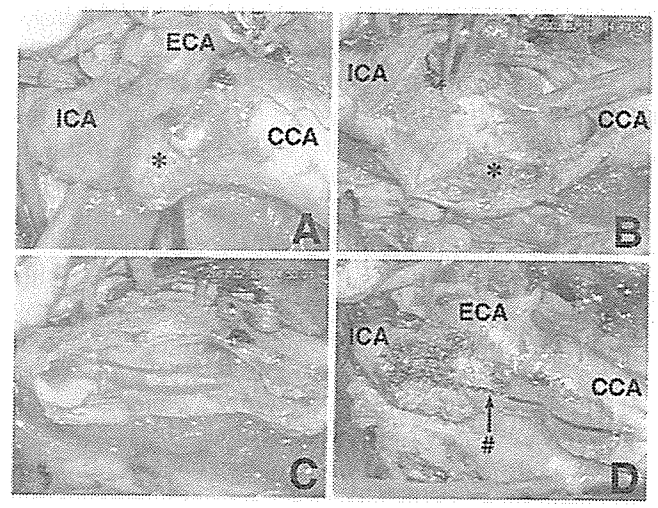

Fig. 2 **Intraoperative photographs of the right carotid artery. A: Appearance of the carotid artery before arteriotomy showing the atheromatous plaque (*asterisk*) projecting from the artery. B: After removal of the bulk of the atheroma showing the residual plaque penetrating the adventitia (*asterisk*) which was removed en-bloc. C: After removal of the protruding atheromatous plaque with the surrounding arterial wall. D: Final view showing arterial closure with a Hemashield patch graft (*sharp*). CCA: common carotid artery, ECA: external carotid artery, ICA: internal carotid artery.**

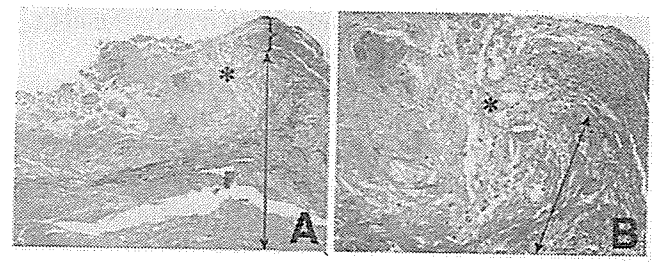

Fig. 3 **Photomicrographs of the protruding atheromatous plaque. A: Atheromatous plaque (*asterisk*) had interrupted the media (*brace*) and invaded the adventitia (*arrow*). Elastica-Masson stain, original magnification ×4. B: Cluster of foamy histiocytes and cholesterin (*asterisk*) had destroyed the collagen fiber of the adventitia (*arrow*). Elastica-Masson stain, original magnification ×10.**

was intermediate and there was no indication that the atheroma protruded out of the adventitia. CEA was planned according to the surgical indications for symptomatic patients.[6,7] However, since preoperative screening with coronary arteriography revealed severe stenosis of the left descending artery, percutaneous transluminal angioplasty was first performed in another hospital.

Twelve weeks after the coronary intervention and 22 weeks after the onset, CEA was performed under somatosensory evoked potential (SEP) and regional cerebral oxygen saturation (rSO_2) monitoring from the bilateral frontal and right temporal regions. On reaching the carotid bifurcation, a yellowish mass was observed protruding out of the vessel wall (Fig. 2A). The mass appeared to be fragile atheromatous plaque and the adventitia over the mass had disappeared over an area of 5 mm in diameter. The atheroma seemed to penetrate the adventitia and was only covered with loose connective tissue. Care was taken not to injure the fragile atheroma before the carotid artery could be dissected proximally and distally for temporary occlusion.

After systemic heparinization, endarterectomy was performed during temporary occlusion of the carotid system. The arterial incision was made longitudinally avoiding the protruding atheroma (Fig. 2B). Since SEP and rSO_2 monitoring detected no change, no shunt was used during the occlusion. The yellowish mass was totally removed from the

carotid wall to form an oval orifice surrounded by the endarterectomized media-adventitia (Fig. 2C). Then a collagen-impregnated polyester patch graft (Hemashield patch™; Boston Scientific, Ballybrit Business Park, Galway, Ireland) was used for arterial closure (Fig. 2D).

Histological examination of the resected carotid artery found marked atherosclerosis with thickening of the intima by fibrosis and atheroma plaque consisting of foamy histiocytes and cholesterin (Fig. 3). The media had completely disappeared and the adventitial collagenous tissue was penetrated by the atheroma in the yellowish mass, confirming that the mass was part of the atheroma.

The postoperative course was uneventful and he left hospital 14 days after the surgery with no new neurological deficit.

Discussion

One of the major hypotheses for the pathogenesis of atherosclerosis is called the "response to injury" hypothesis, which suggests that atherosclerosis is a chronic inflammatory response of the arterial wall initiated by injury to the endothelium.[9] Chronic endothelial injury leads to increased permeability, leukocyte adhesion, and higher thrombogenic potential. Monocytes and leukocytes migrate into the intima and are transformed into macrophages and foam cells. Then smooth muscle cells migrate from the media into the intima and proliferate in the intima. Finally, lipids accumulate within the cells as well as extracellularly.

Atheroma in the cervical carotid arteries is generally formed in the intima but often involves the media. However, atrophy of the underlying media with loss of elastic tissue in advanced plaque causes weakness of the arterial wall.[9] Unstable plaques of the carotid artery show histological evidence of collagen and elastic fiber fragmentation.[2] In our case, the histological findings showed that the media was interrupted and foamy histiocytes and cholesterin had extended from the adventitia into the connective tissue. Therefore, we suspected that such media and adventitia weakening may have been involved in the mechanism of atheroma protrusion.

In this case, even retrospective peer review found no preoperative radiological evidence to suggest that the atheroma in the carotid artery had penetrated the vessel wall. Methods which could depict such plaque advancement include carotid duplex scanning, intravascular ultrasonography,[1,5] black blood magnetic resonance imaging,[10] optical coherence tomography (OCT),[4] and others. The first three methods do not have sufficient resolution to demarcate the adventitia clearly at present. OCT is a new imaging method with a high resolution of approximately 10–20 μm. OCT imaging showed the intima, media, and adventitia in a case of coronary stenosis with good correlation of the intimal thickness measured by OCT and histological examination. However, the maximum depth of penetration of OCT is approximately 2.0 mm from the center of the catheter.[4]

The present case appears to be the first to illustrate penetrating atheroma in the carotid artery and shows that careful dissection of the carotid artery is essential if the carotid wall is unusually colored, to prevent premature disintegration of the fragile atheroma. Primary arterial closure may not be possible after removal of the plaque, so patch graft closure should be considered to maintain adequate arterial lumen. To minimize the temporary occlusion time, a patch graft should be prepared before carotid clamping.

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原　著

もやもや病に対するSTA-MCA吻合術後・過灌流と一過性神経脱落症状について
—IMP SPECTを用いた検討—

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Transient Focal Neurological Deficit Due to Hyperperfusion after Superficial Temporal Artery-Middle Cerebral Artery Anastomosis in Patients with Moyamoya Disease

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Summary: Surgical revascularization for moyamoya disease is believed to prevent cerebral ischemic attacks by improving cerebral blood flow (CBF). We investigated how the rapid increase in CBF through the direct bypass affects the ischemic brain.

CBF was measured by N-isopropyl-p-[^{123}I] iodoamphetamine single-photon emission computed tomography (^{123}I-IMP-SPECT) within 1 week after superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis performed on 27 sides of 22 consecutive patients (male:female＝6:16, 2–62 years old) with moyamoya disease from March 2004 to April 2005. Five patients (male:female＝1:4, 26–55 years old) suffered delayed transient focal neurological deficit mimicking ischemic attack at 2 to 7 days after surgery. Postoperative SPECT revealed focal intense increase in CBF at the sites of anastomosis in all 5 patients. Postoperative magnetic resonance imaging showed no ischemic changes, and magnetic resonance angiography showed the apparently patent STA-MCA anastomosis as thick high signal intensity sign in all 5 patients. The anatomical location and the temporal profile of hyperperfusion were completely in accordance with the neurological deficits. Strict blood pressure control and administration of a free radical scavenger were instituted. The symptoms were resolved in all patients.

In conclusion, transient focal neurological deficit following STA-MCA anastomosis can be caused by focal hyperperfusion in patients with moyamoya disease. Routine CBF measurement is recommended to differentiate hyperperfusion and transient ischemic attack, since the treatments for these conditions are contradictory.

Key words:
- moyamoya disease
- superficial temporal artery-middle cerebral artery anastomosis
- hyperperfusion
- single-photon emission computed tomography

Surg Cereb Stroke (Jpn) 34: 37–41, 2006

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はじめに

もやもや病は両側内頸動脈終末部，前およびに中大脳動脈近位部が進行性に狭窄・閉塞し，その付近に異常血管網の発達を認める原因不明の疾患である[10]．浅側頭動脈・中大脳動脈(STA-MCA)吻合術は本疾患による脳虚血を改善するための有効な治療法として広く用いられている[3)8)]．一方，もやもや病患者においてはバイパス術後に神経学的症状が大きく変動することもあり，脳虚血発作による一過性の局所神経脱落症状を呈することもまれでないと考えられてきた[4)7)]．しかしながらこれら周術期の神経脱落症状の原因となる病態の詳細は不明である．またもやもや病に対するバイパス術による急激な血流増加が脳循環代謝に与える影響についても不明な点が多い．本報告では当施設において最近STA-MCA吻合術を施行したもやもや病連続症例の中で，バイパス術後に術後過灌流による一過性局所神経脱落症状を呈した5例を報告する．術後の一過性神経脱落症状は虚血発作に類似していたが，全例でN-isopropyl-p-[^{123}I] iodoamphetamine (^{123}I-IMP-SPECT)により局所神経脱落症状の責任病巣として矛盾しない吻合部周囲に限局した過灌流を認めた．

対象と方法

対象は平成16年3月から17年4月まで当施設にてSTA-MCA吻合術を施行したもやもや病・連続27側・22例(男/女＝6/16，2-62歳，平均34.5歳)である．2例の片側症例と神経線維腫に合併した類もやもや病1例を除いて全例，厚生労働省ウイリス動脈輪閉塞症診断基準を満たしている．全症例においてSTA-MCA吻合術を含めた血行再建術を施行した．初期の4例を除いてencephalomyosynangiosis (EMS)にdural pedicle insertionを加えた間接血行再建術を追加した[8)]．手術は原則として症候性であり術前IMP SPECTにて脳血流の低下と脳循環予備能の低下が認められたものに対して施行している．recipient arteryには原則として頭頂葉に向かうM4 (anterior parietal artery)を用いている．可能な症例では赤外線画像装置(Intrared imaging system: IRIS-IV, Sparkling Photon Inc., Tokyo, Japan)による吻合前後の術中脳表モニタリングを行った．全例で術後急性期(第1-2病日，第6-7病日)に^{123}I-IMP-SPECT (ARG法)により脳血流の定量を行い，各関心領域の脳血流を3DSRT-version 2.0(第一ラジオアイソトープ)にて解析した．脳実質の術後変化，バイパスのpatencyは1.5 Teslaのmagnetic resonance imaging (MRI)/ magnetic resonance angiography (MRA)にて術後2-3日目，ならびに10-14日目に評価した．MRIについてはT1，T2強調画像に加えて拡散強調画像，fluid attenuated inversion recovery (FLAIR)とT2*強調画像による評価を行った．術後急性期の臨床症状と放射線学的検査結果の経時的変化との関連を検討した．

結　果

術直後に神経学的脱落症状を呈した症例は麻酔覚醒時に5分間，一過性の術反対側大脳半球の虚血症状を呈した1例を除いてみられなかった．5例・5側において術後経過中，遅発性に一過性脳虚血発作(TIA)に類似した一過性・局所神経脱落症状を認めた(男：女＝1：4，26-55歳)．5例全例で術後SPECTにて吻合部の皮質に局所的高灌流域を認め，この高灌流域の局在は局所神経脱落症状の責任病巣として矛盾しなかった．MRI/MRAでは5例全例でSTA-MCAバイパスは太く描出され，吻合部位周囲皮質にはFLAIRにて線状の高吸収域を認めた．拡散強調画像にて虚血巣を認めた症例はなかった．血圧コントロール(降圧)，ならびに抗酸化剤(エダラボン)の使用にて5例全例で局所神経脱落症状は改善した．22例・27手術を通して，退院時にあらたな神経学的脱落症状を残した症例はなかった．過灌流による一過性局所神経脱落症状を呈した5

Table 1 Summary of 5 cases with transient focal neurological deficit due to hyperperfusion

Case No.	Age/sex	Type	Side of operation	Symptoms	Period of deficit	Hyperperfusion by SPECT
1	38/F	infarction	left	aphasia	POD 2-6	POD 1, 7
2	55/F	hemorrhage	right	dysarthria, numbness	POD 7-20	POD 6
3	36/F	TIA, seizure	left	aphasia	POD 2-14	POD 1 *, 7
4	37/M	infarction	right **	aphasia	POD 4-60	POD 2, 7
5	26/F	TIA	right	dysarthria, facial palsy	POD3-12	POD1 *, 7

M: male, F: female, POD: postoperative day, SPECT: single-photon emission computed tomography, TIA: transient ischemic attack.
* Slight increase at the site of the anastomosis.
** Language dominancy in the right hemisphere as shown by functional magnetic resonance imaging.

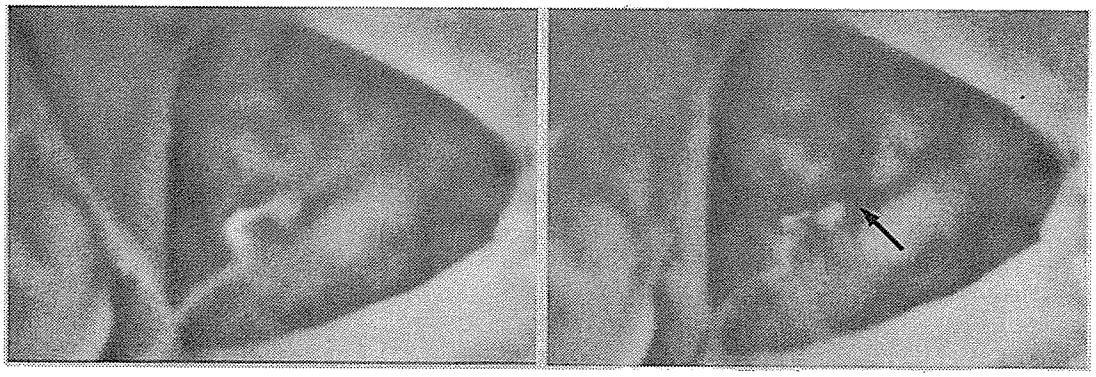

Fig. 1 Case 5. Monitoring of the cerebral surface flow dynamics using Intrared Imaging System: IRIS-IV (Sparkling Photon Inc., Tokyo, Japan) before (A) and after (B) STA-MCA anastomosis, showing significant increase of cerebral blood flow around the site of anastomosis (arrow in B) as shown by black color. A|B

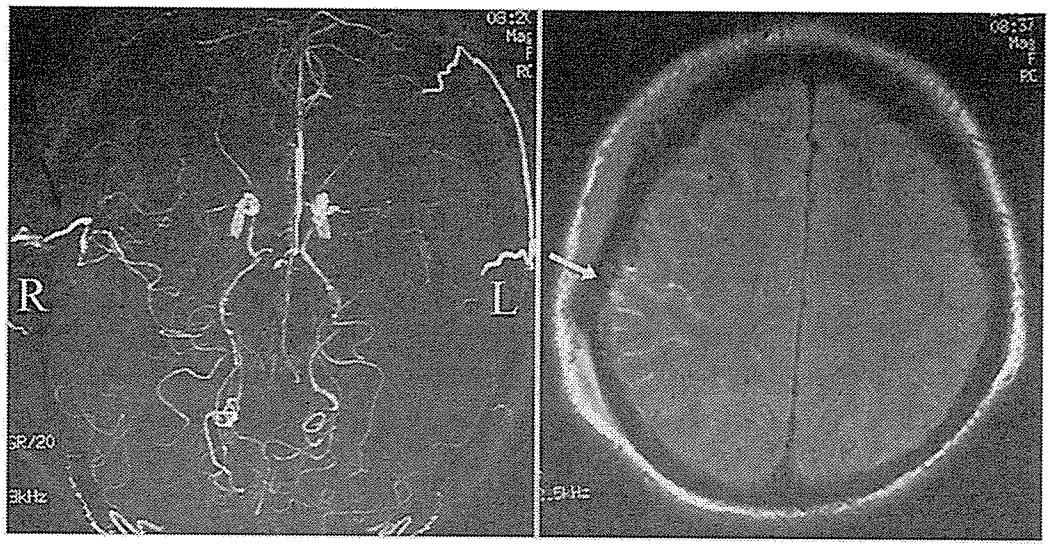

Fig. 2 Case 5. Postoperative magnetic resonance angiogram showing the apparently patent STA-MCA bypass as a thick high signal intensity sign (A). Fluid attenuated inversion recovery showed laminar high signal intensity at the site of anastomosis (arrow in B). R: right, L: left A|B

例のまとめを Table 1 に示す.

(代表症例：症例5) 26歳，女性.

平成16年8月頃より左上肢の脱力発作が出現．近医にてもやもや病が疑われ当科紹介，血行再建術目的に入院となった．神経学的脱落症状なく，脳血管撮影では両側・3期[10]のもやもや病を認めた．術前SPECTでは両側大脳半球の血流低下と脳循環予備能の低下を認めた(右側がsteal現象あり)．17年3月に右STA-MCA吻合術と間接血行再建術を施行した．頭頂葉に向かう0.8 mmの皮質動脈(M4)にSTA(直径1.0 mm)を吻合した．赤外線画像装置IRIS-IV (Sparkling Photon Inc., Tokyo, Japan)による術中脳表モニタリングでは吻合後のSTAクランプ解除直後より吻合部周囲に黒色で示されるように皮質枝の血流の著明な上昇を認めた(Fig. 1)．術直後，神経学的脱落症状を認めず術後MRI拡散強調画像でも虚血巣の出現は認めなかった．術後MRAではバイパスは太く描出されており patency が確認された(Fig. 2A)．術翌日の安静時SPECTでは吻合部位である左側頭・頭頂葉に脳血流の増加を認めた(Fig. 3B)．術後2日目のMRI (FLAIR)では吻合部位周囲に脳溝に沿った線状の高信号を認めた(Fig. 2B)．術後3日目より術直後にはみられなかった左上肢の感覚障害，構語障害と左顔面麻痺が出現した．術後7日目のSPECTでは右側頭・頭頂葉に限局した高灌流はさらに増加していた(Fig. 3C)．MRI (FLAIR)でも吻合部位周囲に脳溝に沿った線状の高信号は顕著となった．抗酸化剤と降圧剤にて加療を行ったところ症状は徐々に改善し術後12日目には完

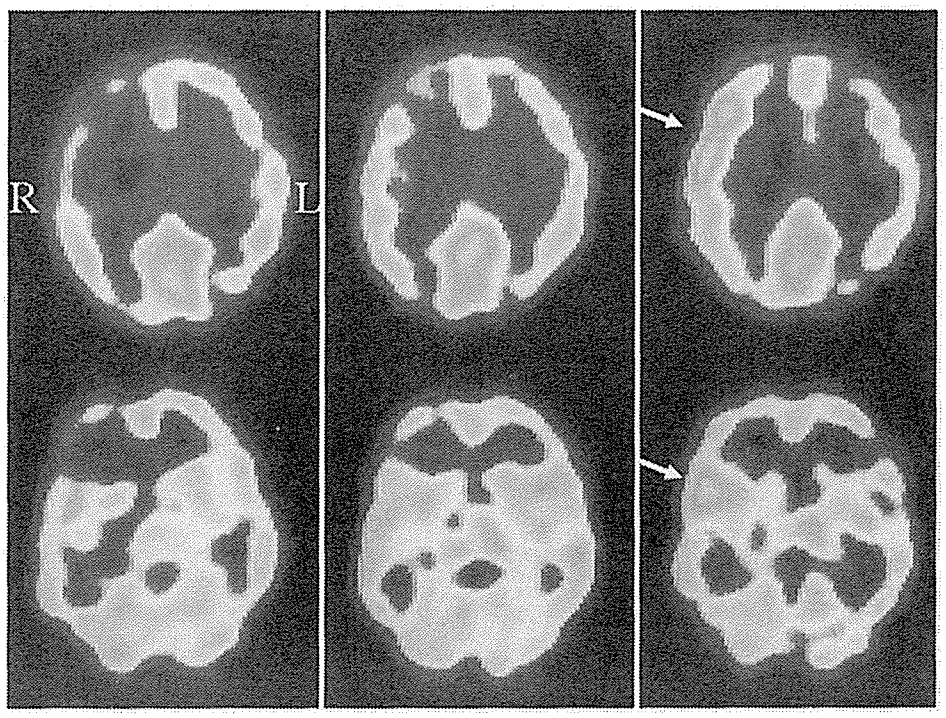

Fig. 3 Case 5. ^{123}I-IMP-SPECT scans before surgery (A) and 1 (B) and 7 days (C) after surgery. Mild increase in CBF was detected on the side of anastomosis 1 day after surgery. The focal intense increase in CBF at the site of anastomosis (arrows in C) was evident 7 days after surgery, in accordance with the manifestation of dysarthria and facial palsy. R: right, L: left

A|B|C

全に消失した．術後13日目に新たな神経学的脱落症状なく独歩退院した．

考　察

今回提示した5症例におけるバイパス術後の一過性局所神経脱落症状の原因は，以下の理由で術後過灌流によるものと考えられた．(1) 術直後にはみられなかった局所神経脱落症状の出現に先立ってSPECTにより術側の血流増加を認めた．(2) 血流の増加は局所神経脱落症状の責任病巣として矛盾しない吻合部位に限局していた．(3) 術後MRAにて術側にthickなSTAの描出と脳表の血管へのflowが確認され，拡散強調画像でも新たな虚血病変がみられなかった．(4) 局所神経脱落症状の経過に沿って過灌流域に一致してMRI FLAIRにて脳溝に沿った高信号域を認めた．

もやもや病以外の閉塞性脳血管障害に対する頸動脈内膜剥離術(CEA)やSTA-MCA吻合術後においては，慢性虚血脳に対する急激な血流上昇による「過灌流症候群」[9]を呈することがまれではない．一方，もやもや病においては術後の虚血発作についてはまれでないと考えられてきた反面[4)7)]，術後過灌流による神経症状発現の可能性についてはほとんど検討されてこなかった[2)]．今回のわれわれの連続22例・27手術症例の検討においては，術後遅発性に，明らかな一過性局所神経脱落症状を呈した5例はすべて吻合部位に限局した過灌流を呈していた．非もやもや病患者に対するSTA-MCAバイパス後も同様のSPECT所見をまれならず認めるにもかかわらず，頭痛や痙攣を伴わず過灌流による局所神経脱落症状を呈する例はまれであることを考えると，5症例で認められた過灌流による臨床症状発現はもやもや病に特異的な反応である可能性がある．

今回の5症例においてはSPECTにて過灌流の病態への関与が明らかであったため降圧，抗酸化剤の投与により神経学的脱落症状を残すことはなかった．しかし臨床症状のみからは虚血発作との鑑別はいずれも困難であり過灌流に対する適切な診断，対処がもやもや病血行再建術後には不可欠なものと考えられた．さらにはもやもや病における術後過灌流の予測因子の解明が望まれる．術前SPECTにおける脳循環予備能，解剖学的な血管構築，年齢，発症形式などの関与が推測される．なお，今回のわれわれのシリーズには8歳以下の小児例が5例含まれているが術後過灌流による臨床症状は呈さなかった．年齢も含めた因子の関与については今後症例数を増やし，さらなる検討が必要と考

えられる．

過灌流による特異的な臨床症状の発現に関してはもやもや病特有の脳血管における分子発現，過灌流時の活性酸素の発現量の違い，活性酸素に対する反応の違いが寄与している可能性がある[5]．過灌流症例における髄液中，血中の蛋白発現の変化について検討することにより病態解明の糸口がつかめるかもしれない．また神経細胞死(necrosis)に至らない程度の活性酸素の産生も長期的にはシグナル伝達経路を介したアポトーシスを惹起することが知られており[1]，今回のような一過性神経脱落症状を呈した症例の長期的な脳機能的予後についても興味が持たれるところである．実際，CEA後に過灌流症候群を呈した症例では術後長期の高次脳機能が低下していることが報告されている[6]．なお，今回報告した5例の中でも1例で術後長期のMRIにて過灌流部位に一致したatrophic changeを認めており長期的な器質的変化についても現在検討中である．

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