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Emergent Carotid Artery Stenting Following Intravenous Alteplase Infusion After Rapid Negative Diagnosis for COVID-19 by Loop-Mediated Isothermal Amplification Assay

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Key words
- Acute ischemic stroke
- Alteplase
- Carotid artery stenting
- COVID-19
- Emergency
- LAMP assay

Abbreviations and Acronyms
AIS: Acute ischemic stroke
CAS: Carotid artery stenting
COVID-19: Coronavirus disease 2019
CT: Computed tomography
eCAS: Emergent carotid artery stenting
Fr: French
hAIS: Hyperacute ischemic stroke
ICA: Internal carotid artery
ICS: Internal carotid artery stenosis
LAMP: Loop-mediated isothermal amplification
MRI: Magnetic resonance imaging
PFC: Proximal flow control

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BACKGROUND: **During the coronavirus disease 2019 (COVID-19) pandemic, a rapid screening method for COVID-19 detection is needed to decide the appropriate strategy to treat stroke patients. In acute ischemic stroke treatment, the efficacy and safety of emergent carotid artery stenting (eCAS) for hyperacute ischemic stroke (hAIS) due to internal carotid artery stenosis (ICS) have not been sufficiently established.**

CASE DESCRIPTION: **A 71-year-old man with hAIS caused by severe ICS was treated via intravenous alteplase infusion. The patient underwent screening for COVID-19 by the loop-mediated isothermal amplification (LAMP) assay shortly after arrival at our institution. The LAMP result was obtained within 90 minutes, during intravenous alteplase infusion, and turned out to be negative. The symptom of hemiplegia worsened during alteplase infusion, and he, therefore, underwent eCAS after administration of aspirin (200 mg). Recanalization was achieved successfully by eCAS, and dual antiplatelet therapy and argatroban were administrated following eCAS. Hemorrhagic complications or restenosis/occlusion of the carotid artery were not observed. He was discharged without neurologic deficits 15 days following eCAS. Because of the rapid negative diagnosis for COVID-19 using the LAMP method, eCAS could be performed following standard procedures, along with infectious defense, without delay.**

CONCLUSIONS: **This case report suggests that eCAS for hAIS due to ICS following intravenous alteplase can be an effective treatment, along with appropriate antiplatelet medication and management in select patients. During the COVID-19 pandemic, the LAMP assay for COVID-19 detection might be a suitable diagnostic strategy preceding stroke treatment because of the rapid turnaround time.**

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has had a significant impact on treatment paradigms of all diseases.[1-4] For instance, patients with acute ischemic stroke (AIS), who must be treated appropriately and promptly, should be screened for COVID-19 simultaneously.[5-7] Therefore a rapid screening method for COVID-19 is needed to help decide the proper treatment strategy for stroke patients.

Carotid artery stenting (CAS) is a standard treatment procedure for internal carotid artery stenosis (ICS)[8]; however, the efficacy and safety of emergent CAS (eCAS) for hyperacute ischemic stroke (hAIS) due to ICS have not been sufficiently established. Herein, we aimed to report a case of hAIS due to severe ICS, which was successfully treated with eCAS following intravenous alteplase infusion. Moreover, the patient underwent screening for COVID-19 by the loop-mediated isothermal amplification (LAMP) method shortly after admission, and eCAS was performed using standard procedures without any further delay because the LAMP assay revealed a negative diagnosis for COVID-19 immediately before eCAS. This case report demonstrates not only the effectiveness of eCAS for treatment of hAIS but also the value of using the LAMP assay for COVID-19 screening to enable prompt treatment of hAIS.

Case Description

A 71-year-old man was admitted to our institution due to sudden dysarthria and slight left hemiplegia in May 2020. He had a history of atrial fibrillation, hypertension, and diabetes mellitus and had been receiving oral administration of dabigatran. Due to the COVID-19 pandemic, a nasopharyngeal swab specimen collected from the patient was examined using the LAMP assay immediately upon arrival according to the protocol of our institution. The duration from onset to admission was

75 minutes, and the score on the National Institutes of Health Stroke Scale was 6/42. Computed tomography (CT) performed 15 minutes following admission showed a slight ischemic change at the right frontal lobe (Alberta Stroke Program Early Computed Tomography Score: 9). CT angiography demonstrated severe ICS and poor blood flow in the right intracranial internal carotid artery (ICA) (Figure 1A and B). The patient was diagnosed with hAIS due to ICS and was then treated with intravenous alteplase (0.6 mg/kg) (time from onset to infusion: 107 minutes; time from admission to infusion: 32 minutes). Magnetic resonance imaging (MRI) performed during intravenous alteplase infusion revealed sporadic infarction in the right cerebrum (see Figure 1C). The symptoms of hemiplegia improved upon the initiation of intravenous alteplase infusion but got worse again during the alteplase infusion. Thereafter, we decided to perform an eCAS following administration of aspirin (200 mg). As the LAMP assay revealed a negative diagnosis for COVID-19 during intravenous alteplase infusion (time from examination to result: approximately 90 minutes), eCAS could be performed using a standard protection procedure. The flow diagram of the treatment paradigm is described in Figure 2.

The procedure for eCAS was started under local anesthesia 125 minutes after admission. An 8-French (Fr) sheath was inserted into the right femoral artery, and a 6-Fr balloon guiding catheter was positioned in the right common carotid artery. Carotid GuardWire (Medtronic, Minneapolis, Minnesota, USA) was introduced into the ICA, crossing the stenotic lesion, following inflation of the guiding catheter balloon (with proximal flow control, PFC). After performing predilatation, a Carotid Wallstent (Boston Scientific, Natick, Massachusetts, USA) was deployed over the

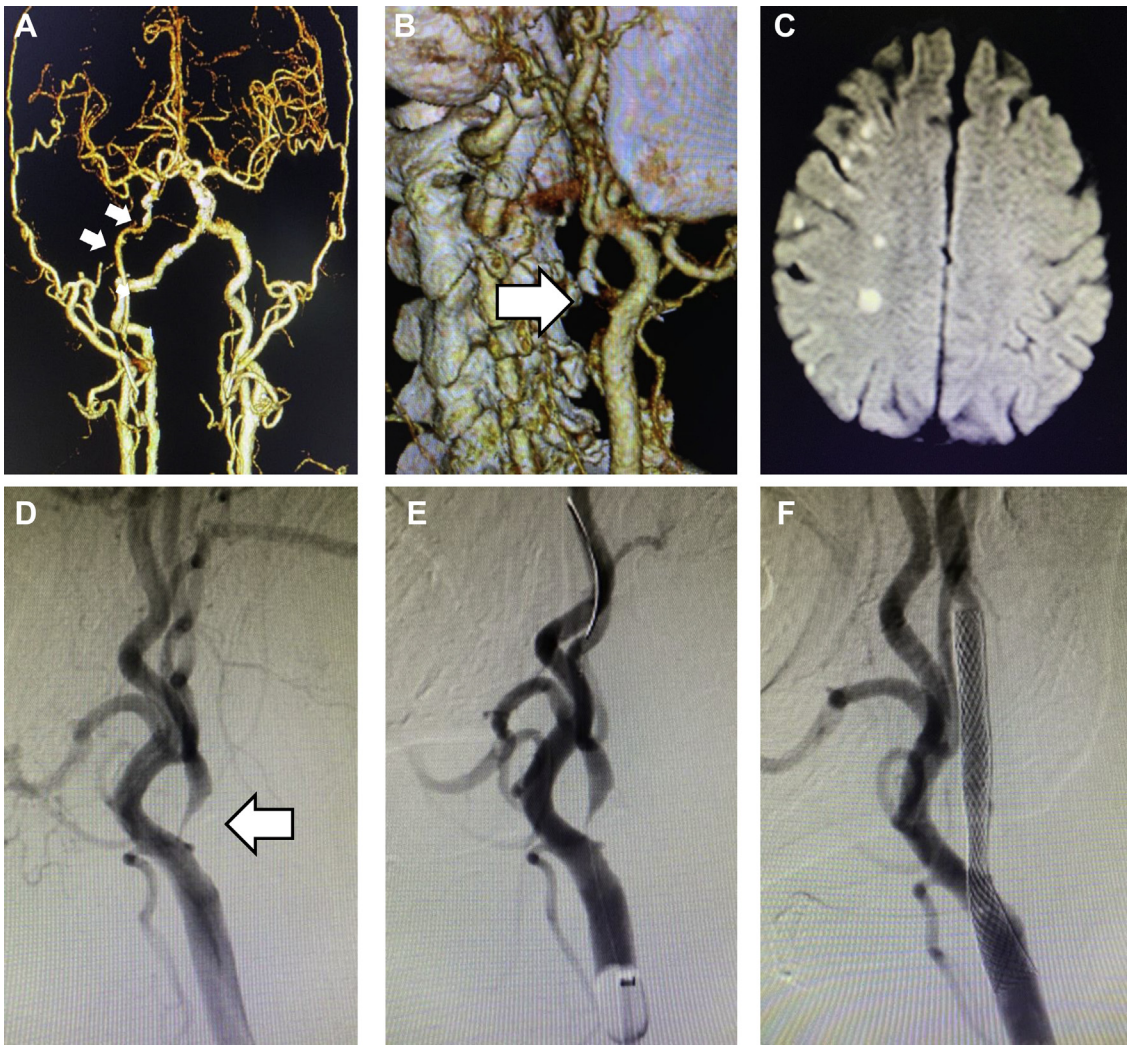

Figure 1. (**A**) Computed tomography angiography showing poor flow in the right internal carotid artery (ICA) (*arrows*). (**B**) Severe stenosis of the right cervical ICA (*arrow*). (**C**) Sporadic infarction on a diffusion-weighted image. (**D**) Before carotid artery stenting angiography (*arrow*). (**E**) Proximal flow control. (**F**) Stent placement.

stenosis and postdilatation was performed (time from puncture to recanalization: 50 minutes) (see Figure 1D–F). After successful recanalization of the ICA by eCAS, the patient was administrated dual antiplatelet therapy (clopidogrel and cilostazol), and apixaban (changed from dabigatran) was continued. Moreover, argatroban and edaravone were administrated 7 days after eCAS. The hemiplegia disappeared, and the National Institutes of Health Stroke Scale score was 0/42 on the day after eCAS. Postoperative CT and MRI showed no evidence of intracranial hemorrhage or ICA occlusion. Ultrasonography performed 1 week after eCAS showed good blood flow of the right ICA. He was discharged from the institute 15 days after admission without neurologic symptoms. MRI performed 4 weeks after eCAS demonstrated good blood flow of the right ICA.

DISCUSSION

This case report highlights 2 important findings. First, eCAS following intravenous alteplase infusion for hAIS due to ICS was effective and safe in this patient. Second, the LAMP assay was a suitable screening tool for COVID-19 preceding stroke treatment because the results could be obtained rapidly.

Emergent Carotid Artery Stenting for Hyperacute Ischemic Stroke

Intravenous alteplase has been proven to improve patient outcomes following hAIS,[9,10] and endovascular thrombectomy has become the standard treatment for hAIS due to large vessel occlusion in the anterior circulation.[11-16] However, the efficacy of eCAS for hAIS due to ICS has not been established. Since alteplase is a thrombolytic drug, it cannot be used to treat plaque-based atherosclerotic stenosis. Moreover, chronic atherosclerotic stenosis could not be removed easily by mechanical thrombectomy. Therefore it seems reasonable to assume that eCAS can contribute to recanalization success in patients with hAIS due to ICS. In the present case, we decided to perform eCAS because the symptoms of hemiplegia worsened, despite intravenous alteplase infusion.

While some studies have reported the efficacy and safety of eCAS,[17,18] most of them performed CAS within a few days to 2 weeks following the onset of AIS, and studies demonstrating successful eCAS for hAIS are rare. One of the reasons that the efficacy of eCAS has not been sufficiently ascertained is thought to be the risk of ICA occlusion caused by in-stent thrombosis due to the insufficient efficacy of antiplatelet agents administered before eCAS. Although administration of antiplatelet medication before elective CAS has been recommended, the ideal regimen of eCAS for hAIS has not been established.[19] High-dose antiplatelet medication could decrease the risk of in-stent thrombosis; however, it may increase the risk of intracranial hemorrhage, particularly in patients who have undergone intravenous alteplase treatment. Deguchi et al[20] reported 3 cases of eCAS for hAIS immediately after intravenous alteplase treatment. They administrated antiplatelet agents at the loading dose (cases 1 and 3: 300 mg clopidogrel + 200 mg aspirin; case 2: 300 mg clopidogrel) before eCAS; case 2 presented with an asymptomatic intracranial hemorrhage, and an ICA occlusion due to in-stent thrombosis occurred in case 1. In the present study, the patient was administrated 200 mg aspirin before eCAS, which was less than the dose used in a previous study.[20] The patient presented neither in-stent thrombosis nor hemorrhagic complications. Therefore the dose of antiplatelet agents used or the postoperative management performed in this case might have been appropriate. Additionally, we used Carotid GuardWire and a Carotid Wallstent under PFC. One study has indicated that eCAS for AIS under PFC is effective and safe.[17] This case report provides evidence that could improve the management of eCAS cases following intravenous alteplase infusion. With the recent development of endovascular treatment, effective and safe therapeutic or management strategies for hAIS can be established.

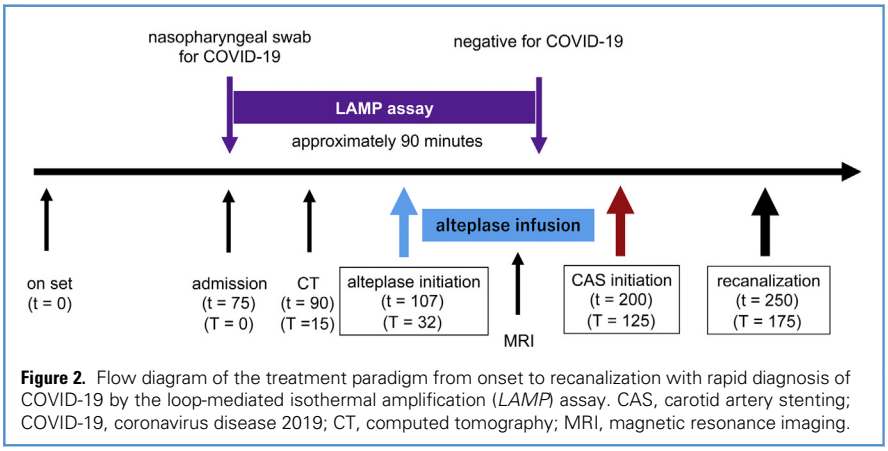

Figure 2. Flow diagram of the treatment paradigm from onset to recanalization with rapid diagnosis of COVID-19 by the loop-mediated isothermal amplification (*LAMP*) assay. CAS, carotid artery stenting; COVID-19, coronavirus disease 2019; CT, computed tomography; MRI, magnetic resonance imaging.

Rapid Screening of COVID-19 Preceding Stroke Treatment

The outbreak of COVID-19 has had a major impact on the treatment of stroke.[1-4,7] Although patients with hAIS should be treated rapidly, physicians have to simultaneously evaluate the patients for COVID-19 infection.[5-7] Real-time polymerase chain reaction is a standard method for COVID-19 detection; however, it takes a long time to obtain the results. Therefore the optimal time window for the treatment of stroke may be exceeded if the physicians wait until a real-time polymerase chain reaction result is known; conversely, stroke treatments performed without waiting for the diagnostic test results for COVID-19 involve risks of nosocomial infections. Practically, stroke treatment might have to be performed under personal protective equipment including N95 respirators.[4,5,7,21] These clinical problems can be overcome if a rapid and simple diagnostic method for COVID-19 screening can be developed. In the case presented here, we used the LAMP assay for COVID-19 screening.

The LAMP assay is a rapid, sensitive, and effective visual nucleic acid amplification method that has been widely applied for the detection of certain viruses.[22-24] The results of the LAMP assay can be obtained in 30 minutes, with high sensitivity and specificity.[22,23] Moreover, the LAMP assay does not

require expensive reagents or instruments.[23] In this case, because the result of the LAMP assay revealed a negative diagnosis for COVID-19 during intravenous alteplase infusion, eCAS could be achieved with standard equipment and procedures according to the protocol of our institute without delay. Thus the LAMP assay might be suitable for COVID-19 detection during stroke treatment because the diagnosis can be rapid. However, some uncertainty remains about whether a negative result on the LAMP assay can confirm whether the patient is truly COVID-19 free; therefore it is advisable to use personal protective equipment, even for patients with a negative diagnosis of COVID-19.[4,5,7,21] Future clinical cohort studies evaluating the LAMP assay for use in COVID-19 screening in clinical practice will be necessary. In addition, in cases that require extremely prompt treatment for stroke when a team cannot wait even for the results of a LAMP assay, it seems unavoidable that one must prioritize the stroke treatment without knowing the patient's COVID-19 infection status while following the appropriate procedures for preventing infection.[4,5,7,21] Rapid and accurate diagnostic methods for detecting COVID-19 should therefore be developed or improved upon urgently.

CONCLUSIONS

This case report demonstrates that eCAS for AIS due to ICS following intravenous alteplase infusion can be an effective treatment option along with appropriate antiplatelet medication and management in select patients. During the COVID-19 pandemic, the LAMP assay for COVID-19 detection might be a suitable diagnostic method preceding stroke treatment because the diagnosis can be made rapidly.

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