Is Acute Carotid Artery Stent Thrombosis an Avoidable Complication?

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The most serious complication of carotid artery stenting (CAS) is acute carotid artery stent thrombosis (ACAST). ACAST is a very rare complication, but it may lead to dramatic and catastrophic consequences. The most important cause is inadequate or ineffective antiaggregant therapy. It is very important to identify, before CAS, those patients who might be candidates for ACAST and to start antiplatelet therapy for them. Testing patients who are candidates for CAS for acetylsalicylic acid and clopidogrel resistance may prevent this complication. **Key Words:** Antiplatelet resistance—carotid artery stenting—stent thrombosis—stroke.

Carotid artery stenting (CAS) is an alternative to carotid endarterectomy (CEA) for primary and secondary prevention of ischemic stroke. The most serious complication of CAS is acute carotid artery stent thrombosis (ACAST). The treatment approach for patients who develop ACAST is still controversial. Regardless of which treatment method is used, ACAST may lead to serious neurologic deficits in patients and even to death. Procedure-related complications, operator-related causes, and mechanisms of cellular thrombosis are inculpated in the etiology of ACAST.[1]

It is very important to identify, before CAS, those patients who might be candidates for ACAST and to give them appropriate antiplatelet therapy. It is difficult to predict the operator-related and procedure-related complications. However, it is possible to identify in advance those patients who may develop ACAST due to antiplatelet resistance. This article presents the discussion about 3 patients who developed ACAST due to antiplatelet resistance, 1 patient who developed ACAST due to irregular use of antiplatelet drugs, and 4 patients who were found to have antiplatelet resistance before CAS and were given an antiaggregant therapy other than clopidogrel and were thus prevented from developing ACAST.

Cases and Carotid Artery Stenting

In our clinic, a council of physicians from the neurology, cardiology, cardiovascular surgery, and radiology departments evaluates the patients who have carotid artery stenosis and plans their treatment accordingly. CAS has been performed for 192 of all patients who have been evaluated by the council so far. CAS procedure has been routinely performed through transfemoral access. CAS procedure was initiated by performing a diagnostic arcus aortography. This was followed by carotid angiographies and bilateral cerebral angiography. When the procedure was terminated, the bilateral cerebral angiography was repeated so that possible distal embolization could be ruled out. In all CAS procedures, cerebral embolism prevention device was used, and 75u/kg unfractionated heparin was given through femoral artery. Activated clotting time was kept at around 250 seconds during the entire procedure. Balloon postdilation of more than 8 atm was performed for 8 patients after stenting. The systemic blood pressure values of the patients were stable during the procedure. All procedures were finalized without complications.

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Results

The demographic, clinical, radiological, laboratory, and pharmacological characteristics as well as complications of all patients are presented in chronological order in the tables (Tables 1 and 2). Abbott-Vascular Xact Stent (Abbott Vascular, Santa Clara, USA) was used for the first, sixth, seventh, and eighth patients, Cristallo Ideale SE Stent (Invatec, Roncadella (BS), Italy) was implanted to the fourth patient, and sinus-Carotid-Conical-RX Stent (OptiMed, Ettlingen, Germany) was used for the second, third, and fifth patients. As a carotid balloon, Pyxis-c-Balloon Catheter (QualiMed, Winsen, Germany) was chosen. At least 1 week before the CAS procedure, all patients were given 100 mg of acetylsalicylic acid (ASA) and 75 mg of clopidogrel, peroral. The first 3 patients were found to be resistant both to ASA and to clopidogrel. Their antiplatelet resistance was detected after the development of ACAST. The fourth patient did not have an antiplatelet resistance. But the patient discontinued clopidogrel. Therefore, his P2Y level was found to be 85 seconds. His P2Y level was found to be 228 seconds in 24 hours after 600-mg loading dose of clopidogrel given to the patient. Clopidogrel therapy was continued, and the patient's P2Y level before the CAS procedure was more than 228 seconds. The fifth, sixth, seventh, and eighth patients were not found to have resistance to ASA in pre-CAS resistance tests whereas they had resistance to clopidogrel. One day before the CAS procedure, these patients were given 180-mg loading dose and maintenance dose of 90 mg bid of another adenosine diphosphate (ADP) receptor blocker, which was ticagrelor. The CAS procedures were finalized without complications. Patients who undergo CAS procedure in our center are given a 1-year dual therapy of antiplatelet agents. We have started to use CEA therapy for patients who have resistance both to ASA and to clopidogrel since our experience with ACAST caused by dual antiplatelet resistance. Patients who underwent CEA were given 90 mg bid of ticagrelor for a whole month. Those patients who are resistant to clopidogrel only, however, are given a loading and maintenance dose of ticagrelor in our center, after which CAS procedure is performed.

All the ACAST patients were followed in our clinic for 3-4 hours following the CAS procedure. The peak effect of unfractionated heparin is reached in 2 to 4 hours. Keeping in mind the time spent during CAS procedure, we can conclude that ACAST developed after the peak effect of unfractionated heparin was reached.

No other cellular etiologic explanation could be found in our ACAST patients. Platelet and neutrophil counts were in the normal range. Hematologic examination revealed no blood coagulopathy including protein C deficiency, protein S deficiency, antiphospholipid antibody syndrome, or homocystinemia. We detected no mutation of factor V Leiden, prothrombin 20210, or antithrombin III.

Discussion

When we analyzed those patients having ACAST and those who were candidates of ACAST but found to have antiplatelet resistance before CAS and prevented from developing acute thrombosis, we revealed the following findings: Although we made CAS process for the first 3 patients, antiplatelet resistance could not be evaluated before CAS. We found dual antiplatelet resistance in these patients in the analysis we performed to find the possible cause after ACAST. Then we gave 100-mg ASA and 75-mg clopidogrel to all patients for 1 week before CAS and analyzed antiplatelet resistance routinely. We preferred CEA for those patients who had dual antiplatelet resistance. Those patients who had resistance only to clopidogrel (patient no. 5-8) were given a loading dose of 180 mg of ticagrelor, which was another group of ADP receptor blocker, at least 1 day before the CAS procedure and we continued the treatment with 90 mg twice daily. ASA and ticagrelor were continued for 1 year following the CAS procedure.

ACAST is a rare complication but has a high morbidity and mortality rate. Its incidence ranges from .04% to 2%.[2] Its etiology is multifactorial and could not be fully revealed. The possible causes include drug interaction, drug compliance, genetic polymorphism, and individual biological and inflammatory factors. Antiplatelet resistance is an important etiological factor[3] that can be

Table 1. *Demographic features of the patients*

Patient no.	Sex	Age (y)	Hypertension	Diabetes mellitus	Coronary artery disease	Smoker	Statin use	Platelet count (10^3/μL)	MPV (fl)
1	Male	74	+	−	+	−	−	252	10.2
2	Male	73	+	−	+	−	+	265	10.6
3	Male	75	+	+	−	−	−	232	12.8
4	Male	64	+	−	+	+	+	240	11.5
5	Male	72	−	−	+	+	+	179	11.1
6	Male	83	−	−	+	−	+	244	9.2
7	Female	77	+	+	−	−	+	284	9.8
8	Female	45	+	+	+	−	+	242	10.7

Abbreviation: MPV, mean platelet volume.