Progressive Hemorrhagic Transformation Following Dual Antiplatelet Therapy

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Dual antiplatelet therapy (DAT) is often used after endovascular interventional treatment to prevent the recurrence of a stroke. However, DAT may lead to cerebral hemorrhage. We describe two stroke patients with subacute progressive cerebral hemorrhagic transformation (HT) following DAT with aspirin and Plavix. One patient experienced HT 3 weeks after carotid artery stenting that was performed 3 days after an acute stroke; the other patient developed progressive HT within 4 weeks following emergent thrombectomy for acute occlusion of the inferior M2 branch of the right middle cerebral artery (MCA).

The first patient was a 54-year-old male with a history of hypertension and smoking. He was admitted for acute cerebral infarction in the left temporoparietal lobe and received intravenous thrombolysis (Figure 1A). He was found to have significant stenosis in the proximal portion of the left internal carotid artery (ICA) (Figure 1B). Three days after the stroke, the patient underwent successful angioplasty (4 × 20 mm Sterling Monorail balloon, Boston Scientific, Natick, MA) and stenting (7 × 30 mm Wallstent, Boston Scientific, Natick, MA) of the stenotic left carotid artery (Figure 1C). One week after the procedure, the patient was discharged with partial motor aphasia, right facial palsy, and right limb hemiplegia (upper, grade 0/5; lower, grade 4/5). Aspirin (100 mg qd), Plavix (75 mg qd), and atorvastatin (20 mg qn) were used for secondary prevention. Three weeks after the procedure, the patient complained of dizziness, headache, nausea, and vomit-

Figure 1 (A) Cranial diffusion-weighted images show a fresh infarct lesion in the left temporoparietal lobe; (B) digital subtraction angiography (DSA) shows severe stenosis of the left internal carotid artery (arrow); (C) DSA shows reduction in the stenosis after carotid artery stenting; (D) 17 days after carotid stenting, cranial CT shows hemorrhagic transformation within the existing infarct lesion; (E) 27 days after stenting, repeat CT shows amelioration of the hemorrhage; (F) two months after stenting, cranial CT reveals absorption of hemorrhage.

ing. On physical examination, his blood pressure was 140/80 mmHg, and he was conscious but had motor aphasia, right facial palsy, right upper limb hemiplegia (grade 1/5), and right lower limb hemiplegia (grade 4/5). His left limb muscle strength was normal, and the Babinski sign was negative bilaterally. Cranial CT indicated the presence of cerebral HT within the existing infarct lesion (Figure 1D). Ten days after discontinuation of the antiplatelet drugs, cranial CT revealed absorption of the hemorrhage (Figure 1E), and the patient was discharged. One month later, cranial CT showed further absorption of the hemorrhage (Figure 1F), and aspirin was reinstituted (100 mg qd). At the one-year follow-up, the patient had recovered well, with residual partial motor aphasia and right-sided hemiparesis.

The second patient was a 57-year-old male with a long history of smoking and drinking; he was admitted for sudden left hemiplegia for 4.5 h. On physical examination, his consciousness was clear, and his blood pressure was 170/100 mmHg. The left visual field was defective; muscle strength of the left and right limbs was

0/5 and 5/5, respectively, and he had mixed aphasia. Cranial CT showed no abnormalities (Figure 2A). Cerebral angiography showed occlusion of the inferior M2 segment of the right MCA, which was re-opened by thrombectomy under local anesthesia using a Solitaire AB stent (ev3.4 × 20 mm); a residual stenotic lesion remained (Figures 2B, C). To prevent re-occlusion, DAT (aspirin 100 mg qd and Plavix 75 mg qd) and Lipitor (20 mg qn) were administered. Ten hours after thrombectomy, cranial CT showed a small amount of bleeding. Axial minimum intensity projection of susceptibility-weighted MR imaging (SWI) showed a small HT lesion (Figures 2D, E). SWI showed gradual progression of the HT on post-thrombectomy days 8 and 15 (Figures 2G, H), so DAT was changed to single antiplatelet therapy on day 15 (aspirin 100 mg qd). Twenty-three days after the initial procedure, cranial SWI showed no further increase in the HT (Figure 2I). Three months after the operation, cranial CT showed complete resolution of the HT (Figure 2M). The patient recovered well with partial motor aphasia and right upper limb hemiparesis.

Figure 2 (A) Cranial CT shows no abnormalities at 4.5 h after the onset of the stroke; (B) emergent cranial DSA shows occlusion of the inferior branch of the right middle cerebral artery; (C) after thrombectomy, the occluded branch was reopened; (D) 10 h after thrombectomy, cranial CT shows a small amount of bleeding within a slightly low-density lesion in the right temporo-occipital lobe; (E) at the same time, axial minimum intensity projection of susceptibility-weighted MR imaging (SWI) shows a small hemorrhagic lesion; (F) 24 h after thrombectomy, cranial diffusion-weighted imaging shows a new infarct lesion in the right temporo-occipital lobe; (G) eight days after the operation, SWI shows that the amount of bleeding has increased a little; (H) 15 days after thrombectomy, SWI shows a significant increase in the amount of bleeding (dual antiplatelet therapy is changed to single antiplatelet therapy at this time); (I) 23 days after thrombectomy, cranial SWI reveals no further increase in the amount of bleeding; cranial CT shows gradual absorption of the bleeding after discontinuation of dual antiplatelet drugs as seen at 23 days (J), 27 days (K), and 42 days (L) after thrombectomy; (M) three months after thrombectomy, the hemorrhage has been completely absorbed.

DAT is commonly used following cerebral artery stenting, coronary stenting, and certain other neurointerventional therapies. However, both the use of DAT and the timing of DAT are still controversial. The 18-month-long MATCH study found the addition of aspirin to clopidogrel (Plavix) in stroke patients to be associated with a nonsignificant reduction in major vascular events while increasing the risk of life-threatening or major bleeding [1]. The SAMMPRIS study found a three-month course of DAT to be safe for patients with symptomatic intracranial stenosis [2]. DAT was also found to be safe and effective at reducing stroke recurrence in minor stroke patients when it was used early after stroke onset and switched to single antiplatelet drug at 3 weeks [3].

However, progressive HT occurred in our two cases with 3 weeks of starting DAT. The first case had a medium-sized infarction and severe carotid artery stenosis-related reperfusion injury; these factors may have been related to HT occurrence in this case. Single antiplatelet therapy might have been a better choice in this

case. In the second case, SWI showed mild HT after thrombectomy, and DAT then induced gradual progression of the HT. Therefore, we suggest using single antiplatelet therapy in stroke patients with mild HT on SWI. Monitoring with CT or SWI could be useful during the first 2 weeks of DAT to rapidly diagnose any progression of HT.

Conflict of Interest

The authors declare no conflict of interest.

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