Ischemic stroke in the combined territories of the septum pellucidum and the cingulate gyrus
A case report and literature review
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Abstract
Introduction: Cases of isolated septum pellucidum infarction have not yet been reported. To date, there are only 2 stroke reports involving septum pellucidum infarction. The etiology of septum pellucidum infarction was subcallosal artery (ScA) injury. The abnormalities were strictly confined to the septum pellucidum and the right cingulate gyrus, making this the first case to report such confined abnormalities.

Patient concerns: In this report, we present a case of ischemic stroke confined to the septum pellucidum and cingulated gyrus in a 48-year-old male patient who presented with transient ischemic attack-like paroxysmal left lower limb weakness.

Diagnosis: Even no obvious abnormalities were revealed by an emergency computed tomography, the infarction in the combined territories of the septum pellucidum and the cingulate gyrus was detected on magnetic resonance imaging.

Interventions: Aspirin with clopidogrel was administered for 3 weeks as a secondary preventive drug. Clopidogrel was selected as a long-term antiplatelet drug based on a thromboelastogram.

Outcomes: The patient showed no positive signs related to the nervous system in the hospital, and there was no recurrence during the 3-month follow-up.

Conclusions: Infarction in the septum pellucidum and cingulate gyrus is rare and has atypical clinical manifestations. Physical examination may not yield obvious positive signs. False-negative computed tomography findings of the head may result in misdiagnosis. Thus, it is necessary to perform whole-brain magnetic resonance imaging in time. Moreover, ScA protection should be paid attention to during surgery for anterior communicating artery aneurysm.

Abbreviations: ACoA = anterior communicating artery, AVLT = auditory verbal learning test, CTA = computed tomography angiography, MMSE = mini-mental state examination, MoCA = montreal cognitive assessment, MRI = magnetic resonance imaging, ROCFT = Rey–Osterreith complex figure test, ScA = subcallosal artery, SPT = septum pellucidum tract, TIA = transient ischemic attack, WMS-R = Wechsler memory scale revised.

Keywords: cingulate gyrus, ischemic stroke, septum pellucidum, subcallosal artery

1. Introduction
Septum pellucidum infarction is a rare condition caused by occlusion of one of the branches of the anterior communicating artery (ACoA), also known as the subcallosal artery (ScA). To date, cases of isolated septum pellucidum infarction have not been reported. There have been 2 stroke reports involving the septum pellucidum infarction detected on magnetic resonance imaging (MRI) (Table 1). Here, we report a case of suspected transient ischemic attack (TIA), where MRI revealed infarctions particularly confined to the septum pellucidum and right cingulated gyrus. We have described the evolution of clinical symptoms and presented our hypothesis for the pathogenesis.

2. Methods
Informed written consent was obtained from the patient for publication of this case report and accompanying images. Since the images presented in the article are entirely unidentifiable, the Ethics Committee of our institution waived the requirement for approval of this single case study with medical records.

3. Case presentation
The patient was a 48-year-old man who presented with TIA-like paroxysmal weakness in the lower left limb. In the last 2 days, when the patient became unable to stand properly and perform activities of daily life, he realized that his lower left limb was weak. He could only stand and walk after a rest of 15 minutes, and even then the walk was not proper as he was unable to lift his
## Table 1

| Author-date | Gender-age | History | Clinical features | Infarctions | Etiology | Follow up |
|-------------|------------|---------|------------------|-------------|----------|-----------|
| Moudgil,[1] 2000 | M, 60 | Hypertension | Anterograde amnesia (verbal and visual memory) | Anterior Fo and genu of CC | PAD | 1 mo: significant improvement (short-term memory, verbal and visual memory) |
| Park,[2] 2000 | F, 52 | Hypertension, smoking | Anterograde amnesia (verbal and visual memory) | Bilateral Fo and genu of right CC | PAD | 4 mo: subtle improvement on AVLT, near normal on ROCFT |
| Moussouttas,[3] 2005 | M, 61 | Hypertension, hyperlipidemia, coronary artery disease | Anterograde amnesia | Bilateral anterior Fo, SP and genu of the CC, left frontal subcortical region | PAD | 1 mo: no obvious change |
| Saito,[4] 2006 | M, 71 | Hypertension, smoking, diabetes | Apathy and anterograde amnesia (verbal and visual memory) | Anterior Fo and genu of CC | PAD | 2 mo: short-term memory improvement |
| Hattingen,[5] 2007 | F, 33 | Health | Body of Fo, the adjacent part of the genu and anterior body of CC | Iatrogenic injury after clipping ACoA aneurysm | PAD | 5 wk: cognitive performance improved considerably |
| Goulet,[6] 2008 | M, 68 | Diabetes, hypertension, myoclonus infarction | Acute Korsakoff Syndrome, anterograde and retrograde amnesia | Genu of CC, bilateral anterior columns of Fo | PAD | 1 yr: severe amnesia |
| Adamovich,[7] 2009 | F, 53 | NA | Retrograde and anterograde amnesia | Bilateral anterior Fo | PAD | 2 mo: amnesia persisted |
| Korematsu,[8] 2010 | M, 52 | Smoking | Anterograde and retrograde amnesia, marked decline of delayed recall | Anterior column of the left Fo | PAD | 3 mo: slight improvement (WMS-R: verbal memory 73, visual memory 79, attention/ concentration 93, delayed recall 50, general memory 71) |
| Mosimann,[9] 2012 | M, 47 | NA | Anterograde and retrograde amnesia, parameasias, dysphoria, dysexecutive syndrome, Korsakoff dementia | Bilateral anterior Fo, SP, genu of CC | After ACoA aneurysm clipping | 2 yr: minor progress |
| Murr,[10] 2012 | F, 60 | Hypertension, smoking | Acute confusion and anterograde amnesia | Anterior genu Fo | Giant cell arteritis (biopsy) | NA |
| Rizek,[11] 2013 | M, 56 | AF, stroke, smoking, aortic and mitral valve replacement | Anterograde amnesia | Bilateral Fo | PAD | 4 mo: MMSE 19/30 (recall 0/3), MoCA 12/30 |
| Gupta,[12] 2014 | F, 60 | Paroxysmal AF, embolic stroke, bicuspid aortic valve, prosthetic aortic valve replacement, NSTEMI | Recent retrograde, and anterograde amnesia characteristic of TGA | Body and left column of the Fo | PAD | 12 h: TGA symptoms had resolved |
| Meila,[13] 2015 | F, 59 | NA | Anterograde amnesia | Left anterior Fo | After clipping ACoA aneurysm | NA |
| Meila,[14] 2015 | M, 62 | NA | Anterograde and retrograde amnesia | Bilateral anterior Fo, genu of CC | After clipping ACoA aneurysm | NA |
| Meila,[15] 2015 | F, 32 | NA | Anterograde amnesia | Bilateral anterior Fo, genu of CC | After clipping ACoA aneurysm | NA |
| Meila,[16] 2015 | M, 60 | NA | Memory difficulties, significant cognitive deficits in short-term memory | Anterior Fo, genu of CC | After clipping ACoA aneurysm | NA |
| Meila,[17] 2015 | M, 71 | NA | Korsakoff dementia, attention and concentration difficulties, behavioral troubles | Anterior Fo, genu of CC | After cooling ACoA aneurysm | 6 mo: attention and concentration difficulties as well as behavioral troubles remained |
| Batista,[18] 2015 | F, 56 | Smoking, depression | Disorientation, short-term memory impairment | Anterior columns of both Fo | After clipping ACoA aneurysm | 6 mo: marked improvement in memory deficits, but only mild subsequent improvement over long-term follow-up |
| Orate,[19] 2015 | F, 56 | Smoking | Anterograde amnesia and confabulation | Bilateral anterior columns of the Fo and caudate and lenticular nuclei | PAD | NA |
| Turine,[20] 2016 | F, 74 | Hypertension, right mastectomy | Verbal anterograde amnesia (encoding deficit) and reduced capacities on visual long-term memory | Anterior column of the Fo and posterior part of the CC genu | PAD | 3 mo: the episodic memory disorders did not significantly improve |
| Salvalaggio,[21] 2018 | M, 61 | Hypertension, myocardial infarction, smoking | Anterograde amnesia | Anterior columns of the Fo bilaterally | PAD | |

Amnestic syndrome partially improved
left leg. However, the symptoms were completely relieved after 2 hours of rest. The patient had a prior medical history of hypertension (5 years ago), which was treated with levamlodipine besylate administration. He was an occasional smoker (2–3 times per week), and consumed alcohol (250mL every time) for more than 20 years. On admission, his blood pressure was 140/90mm Hg. He was found to be alert at the time of admission and had no positive signs of nervous system impairment with the National Institutes of Health Stroke Scale score of 0.

No obvious abnormalities were revealed by an emergency computed tomography (CT), and electrocardiography. His serological analysis, including hematologic analysis, and measurement of parameters such as blood sugar, hepatic function, renal function, glycosylated hemoglobin, electrolyte, coagulation function, blood sedimentation, myocardial enzyme, myoglobin, troponin, tumor markers, rheumatism series, folacin, vitamin B12, thyroid function, hepatitis antigens and antibodies, human immunodeficiency virus antibody, and treponema pallidum antibody, were found within the normal limits. However, triglycerides (2.58mmol/L), uric acid (520umol/L), homocysteine (16umol/L) levels were found to be elevated. TIA was suspected, and hence, the patient was treated with aspirin (100mg/d), clopidogrel (75mg/d), atorvastatin (20mg/d).

MRI on a 3.0 T scanner showed abnormal signal for the septum pellucidum and right cingulate gyrus, which was considered to be indicative of acute cerebral infarction (Fig. 1). No atherosclerotic plaque existed in carotid vessels as revealed by ultrasonography reports, and also, no obvious abnormality was found in the transcranial doppler analysis. Moreover, there was no evidence for atrial fibrillation in the 24-hour ambulatory electrocardiogram. Cerebral vessels were assessed by CT angiography (CTA) and it was found that the A2 segment of the right anterior cerebral artery was severely stenosed, along with presence of basilar artery fenestration (Fig. 2). Thromboelastography was performed after 5 days of antiplatelet drug administration to guide secondary treatment. The inhibition rates
of aspirin and clopidogrel were found to be 94.7% and 95.2%, respectively (Fig. 3). Aspirin with clopidogrel was administered for 3 weeks as secondary preventive drug according to the results of the CHANCE study.[30] Clopidogrel was selected as a long-term antiplatelet drug based on the results of thromboelastogram. The patient had no symptoms of neurological damage during 3-month follow-up.

4. Discussion

Septum pellucidum is supplied by ScA, which is the most important branch of ACoA,[19,20] Other branches of the ACoA supply the optic nerves and chiasm, lamina terminalis, hypothalamus, and subcallosal region.[21] Microsurgical anatomy of perforating branches of the ACoA indicates that the perforating branches vary in terms of number, and direction. Corpus callosum has a lower number of perforating branches than the optic chiasma. The ScA is the largest unpaired perforating branch of the ACoA, with a diameter of approximately 0.5 mm, and bilaterally perfuses the medial and ventral cerebral hemispheres (basal forebrain).[22] Therefore, infarctions in the territory of the ScA are mostly associated with bilateral effects. In this case, the cerebral infarctions were confined to the septum pellucidum and cingulated gyrus, which was consistent with the territory of ScA. We speculated hypertension to be the cause of the subcallosal arterial lesion observed in the patient owing to the absence of atherosclerosis evidence, no history of diabetes, or cerebrovascular disease, absence of plaque formation as revealed in the cervical vascular ultrasound, and absence of any significant big vascular stenosis as observed in the head and neck CTA. The etiology was consistent with that of the parent arterial disease subtype in Chinese Ischemic Stroke Subclassification,[24] and small-artery occlusion subtype in Trail of ORG 10172 in Acute Stroke classification.[25] Conventional angiography is difficult to be performed for ScA owing to the 0.5 mm diameter; however, autopsy or surgical microsurgery can be conducted. At present, the visualization of the typical course of ScA was only reported by digital subtraction angiography, and 3D rotational angiography in an AcCoA aneurysm case.[13]

To date, case of isolated septum pellucidum infarction has not been reported. There were 2 reports involving infarction in the septum pellucidum region (Table 1). One of the etiologies was ScA infarction,[3] while the other was a secondary embolization which led to ACoA aneurysm.[9] ScA injury typically causes bilateral fornix infarction (Table 1). Fornix infarction is often characterized by memory impairment which can manifest as anterograde or retrograde amnesia. There are 2 hypotheses to explain this phenomenon:

(1) the fornix is the key structure of the Papez circuit which can be interrupted due to fornix infarction, thereby resulting in memory impairment,[13]

(2) the other hypothesis suggests that memory impairment may be related to the injury of the cholinergic fibers.[26]

Notably, the starting symptoms of the case we report here included paroxysmal weakness of left leg, and absence of amnesia. So far, there have been only 2 reports of infarction in the cingulate gyrus region.[27,28] The clinical manifestations included gelastic seizures, and development of the transient global amnesia. Although the first symptom of our patient was TIA-like paroxysmal lower left extremity weakness, a minor stroke was confirmed later by an MRI analysis. A recent study has successfully identified a novel frontal lobe pathway in the septum pellucidum tract (SPT) connected to the prefrontal cortex.[29] In addition to the right cingulate gyrus, we speculate that this pathway in the SPT may explain the TIA-like symptom.

5. Conclusions

Infarction in the septum pellucidum and cingulate gyrus is rare and has atypical clinical manifestations. Physical examination may not reveal obvious positive signs. False-negative CT findings of the head may lead to misdiagnosis. It is necessary to perform whole-brain MRI in a timely manner. Moreover, ScA protection should be paid attention to during surgery for ACoA aneurysm.
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Author contributions

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Figure 3. Thromboelastography analysis. (A) The platelet inhibition rate of clopidogrel is 95.2% (reference value 30%). (B) The platelet inhibition rate of aspirin is 94.7% (reference value 50%).
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