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**TITLE:** Acute amnesic syndrome in isolated bilateral fornix stroke

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## **Abstract**

**Background.** Acute onset of amnestic syndrome may represent a challenging diagnostic issue. Besides non-vascular etiology, thalamic strokes or infarction involving several temporal lobe structures has been reported. **Patients.** We describe three patients in whom an isolated bilateral anterior fornix infarction presented with an acute amnestic syndrome. Clinical presentation, differential diagnosis and MR images are discussed for each patient and vascular anatomy of the involved brain regions is also considered. **Conclusions.** We suggest that bilateral fornix infarction should always be considered in the diagnostic work-up of an amnestic syndrome with acute onset.

## **Introduction**

Acute onset of persistent amnesia has been reported anecdotally in temporal lobe or thalamic stroke, [1,2] multiple sclerosis [3] and lupus erythematosus [4]. Recently, a few articles described an amnestic syndrome in bilateral fornix infarction detected by MRI [5,6] suggesting that this site of ischemic lesion should be considered in the initial diagnostic work-up of any acute amnestic episode. However, in the few cases in which bilateral fornix

infarction was reported, MRI abnormalities extended also to corpus callosum and anterior cingulate gyrus, and isolated bilateral alteration of the anterior fornix has rarely been described. Vascular etiology involving perforating branches arising from the anterior cerebral artery (ACA) or anterior communicating arteries (ACoA) has been hypothesized (i.e. subcallosal artery) [5,6].

We report on three patients presenting with acute amnesic syndrome who showed MRI abnormalities strictly limited to the anterior columns of the fornix bilaterally. The evolution of clinical symptoms and MRI alterations are described and hypothesis on the pathogenesis is discussed.

### ***Patient 1***

A 61-yr-old man with a medical history of arterial hypertension, hypercholesterolemia, myocardial infarction and smoking presented with acute onset of anterograde amnesia concurrently with a hypertension peak. Except for amnesia, neurological evaluation was unremarkable. Brain CT and doppler ultrasonography of carotid and vertebral arteries were normal. 3T-MRI performed three days after clinical onset showed cytotoxic edema of the anterior columns of the fornix bilaterally (Figure 1A-B). CSF cells count and proteins level were within normal limits. Neuropsychological evaluation demonstrated an amnesic syndrome with confabulation, resembling Korsakoff's syndrome, and deficits of executive functions. Brain 18FDG-PET/MR showed mild glucose hypometabolism at mesial temporal cortex bilaterally. Seven days after the onset of amnesia, the patient had a myocardial ischemia. The diagnostic work-up eventually led also to the detection of a lung cancer. Brain MRI performed one month later showed FLAIR hyperintensity (Fig 1C) and DWI signal

normalization on the fornix columns. Amnestic syndrome partially improved in the following months.

### ***Patient 2***

A 59-yr-old man with a history of arterial hypertension and previous pulmonary embolism due to venous thrombosis was admitted for acute onset of anterograde amnesia with repetitive questions and disinhibition. MRI showed diffusion restriction and FLAIR hyperintensity at anterior columns of the fornix bilaterally. Immunological, infectious, paraneoplastic screening and CSF analysis were unremarkable. Within 4 weeks, MRI follow-up showed normal DWI findings and a mild FLAIR hyperintensity of the fornix. Amnestic syndrome partially improved, while mild amnestic impairment with disinhibited behavior persisted.

### ***Patient 3***

A 74-yr-old Algerian woman presented with acute onset of anterograde amnesia a few weeks after surgical removal of a left VIII cranial nerve schwannoma. Brain 3T-MRI showed symmetric restriction of diffusivity at anterior columns of the fornix and the presence of lipid in subarachnoid spaces (secondary to surgery). Formal cognitive evaluation was not feasible for language barrier. Three weeks later the patient recovered from the amnestic syndrome and MRI showed normal diffusivity and FLAIR hyperintensity within the anterior columns of fornix. MR-angiography showed bilateral narrowing of the anterior cerebral arteries (Figure 1D) consistent with vasculitis or vasospasm likely secondary to chemical meningitis induced by lipid materials in the subarachnoid spaces.

All patients were treated with both anti-platelet drugs and thiamine supplementation although serum B1 levels at admission were within normal limits.

## **Discussion**

The three cases reported represent an amnesic syndrome whose vascular etiology may be easily misdiagnosed in the acute neurological assessment. Vascular etiology is supported by (a) acute onset of symptoms, (b) type and time course of MRI changes, (c) presence of vascular risk factors and comorbidities, such as myocardial ischemia (patient #1), peripheral venous thrombosis and pulmonary embolism (patient #2), or overt intracranial vasculopathy with bilateral severe narrowing of ACA, possibly due to chemical arterial vasospasm (patient #3).

The most common vascular supply of the fornix may be ascribed to a perforating branch of ACoA, namely subcallosal artery. Both microsurgical anatomy and 7T-MRI angiography studies revealed that ACoA gives origin to a major branch (subcallosal artery, in more than 90% of specimens) and a group of small branches [7,8]. Subcallosal artery divides into two terminal stems in up to 45% of specimens. Therefore, it is frequently an unpaired artery that gives rise to branches supplying the corpus callosum, fornix (bilaterally) and hypothalamic regions. When the subcallosal artery does not originate from ACoA, it arises from the proximal A2 segment of ACA [7,8]. Fornix is also supplied by the cisternal segment of lateral posterior choroidal artery and a fornix infarction has been described in vertebral artery dissection (9).

The rarity of fornix involvement in ischemic lesions is explained by its perfusion by branches of the AcoA and also from posterior collateral branches. Notably, in subcallosal artery infarction the lesion extends also to other contiguous structures (i.e. septum pellucidum, genu of the corpus callosum and, anecdotally, anterior cingulate gyrus)<sup>5</sup> while isolated lesion of the fornix is rare and may be due to anatomical variants of arteries supplying this territory.

Other causes of isolated fornix lesion have been ruled out. Patients showed unremarkable blood count, normal liver and renal function, as well as vitamin B1 and B12 serum levels and CSF findings.

Notably, the amnesic syndrome in these three patients was at least in part reversible. Clinical improvement might be explained by an incomplete lesion of the fornices, with preservation of residual functions. Another intriguing hypothesis is the recruitment of alternative memory networks by-passing the fornix. Interestingly, a previous fMRI study on a patient with memory impairment after surgical bilateral transection of the fornices showed that the progressive memory improvement correlated with activation of the orbitofrontal cortex and the middle temporal gyrus (10).

In conclusion, bilateral fornix infarction should be considered in the diagnostic work-up of an acute onset amnesic syndrome. Follow-up memory improvement suggests the possible recruitment of alternative memory-based networks by-passing the column of fornix and the classical circuit of Papez.

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### **Figure legend**

**Fig 1.** Patients 1: appearance of anterior columns of the fornix (arrows) in DWI (A), ADC (B) and FLAIR (C) on 3T MR three days (A-B) and a month (C) after onset of symptoms. Patient 3: 3T MR--angiography showing bilateral narrowing of the anterior cerebral arteries three weeks after onset of symptoms (arrows, D).



Figure 1

