

A case of Post-tPA remote Intracerebral Hemorrhage and significance of Amyloid Angiopathy

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Abstract

Here we present a case of devastating intracerebral hemorrhage after thrombolysis with tissue plasminogen activator (tPA). Interestingly this occurred in an area remote to the original infarct. Magnetic resonance imaging (MRI) of the brain showed numerous micro hemorrhages suspicious for underlying amyloid angiopathy. Post-mortem examination revealed deposition of an amorphous substance in vessel walls, suggestive of amyloid angiopathy that was later confirmed by immunohistochemistry. We discuss the significance of amyloid angiopathy as a risk factor for remote and/or multifocal parenchymal hemorrhages.

Keywords

tPA; amyloid angiopathy; intracerebral hemorrhage

Introduction

Symptomatic intracerebral hemorrhage occurs in approximately 5-6% of patients with ischemic stroke treated with intravenous tPA and carries as high as a 50% risk of mortality [1]. Hemorrhage can occur within the ischemic parenchyma itself (PH) or in areas remote from the infarct (remote parenchymal hemorrhage or PHr) [2]. The incidence of PHr after thrombolysis is approximately 1.3%-3.7% [3]. The mechanism of PHr is not well understood and risk factors appear to be different from that of PH. Patients with PHr are usually older, more often women, have a history of previous ischemic stroke and a lower rates of atrial fibrillation (AF) and diabetes in comparison to patients with PH. Patients with AF presumably have higher rates of PH within the large infarct from thromboembolism. In contrast, it has been suggested that PHr is due to the presence of cerebral amyloid angiopathy(CAA) [2]. A large number of cerebral microhemorrhages on MRI, a radiologic manifestation of CAA, has been shown to increase the risk of PHr after tPA administration [4] but confirmation by autopsy is rarely performed. Despite the higher age of patients with PHr, functional outcome at 3 months is better and mortality is lower compared to in cases of PH [2].

We present a case of post tPA intracerebral hemorrhage in a patient with autopsy confirmed amyloid angiopathy.

Case Presentation

A 73-year-old highly functional man with a history of AF not on anticoagulation, with hypertension and hyperlipidemia presented to an emergency department with sudden onset of aphasia

and right arm weakness. Computerized tomography (CT) scan of the head did not show any evidence of hemorrhage. A clinical diagnosis of acute ischemic stroke was made and tPA was administered. Within two hours, the patient's clinical exam worsened and he became comatose with a Glasgow coma scale (GCS) of 6. He was only able to withdraw all four extremities to painful stimuli. Repeat head CT revealed multiple bilateral intracerebral hemorrhages (Figure 1 A, B). MRI of the brain was obtained which showed bilateral cerebral cortical (Figure 1 C, D) and cerebellar vermis (not shown) hemorrhages. Interestingly, some of the hemorrhages present on gradient echo (GRE) sequence of MRI, were not visible on the CT scan rising suspicion for cerebral micro bleeds. Due to devastating hemorrhage, the patient's family chose to withdraw care and the patient passed away the following day. Autopsy showed extensive amyloid deposition in arterial walls and amyloid plaques in the cerebral cortex (Figure 2). Findings were consistent with cerebral amyloid angiopathy, multiple hemorrhages, and early Alzheimer's disease.

Figures

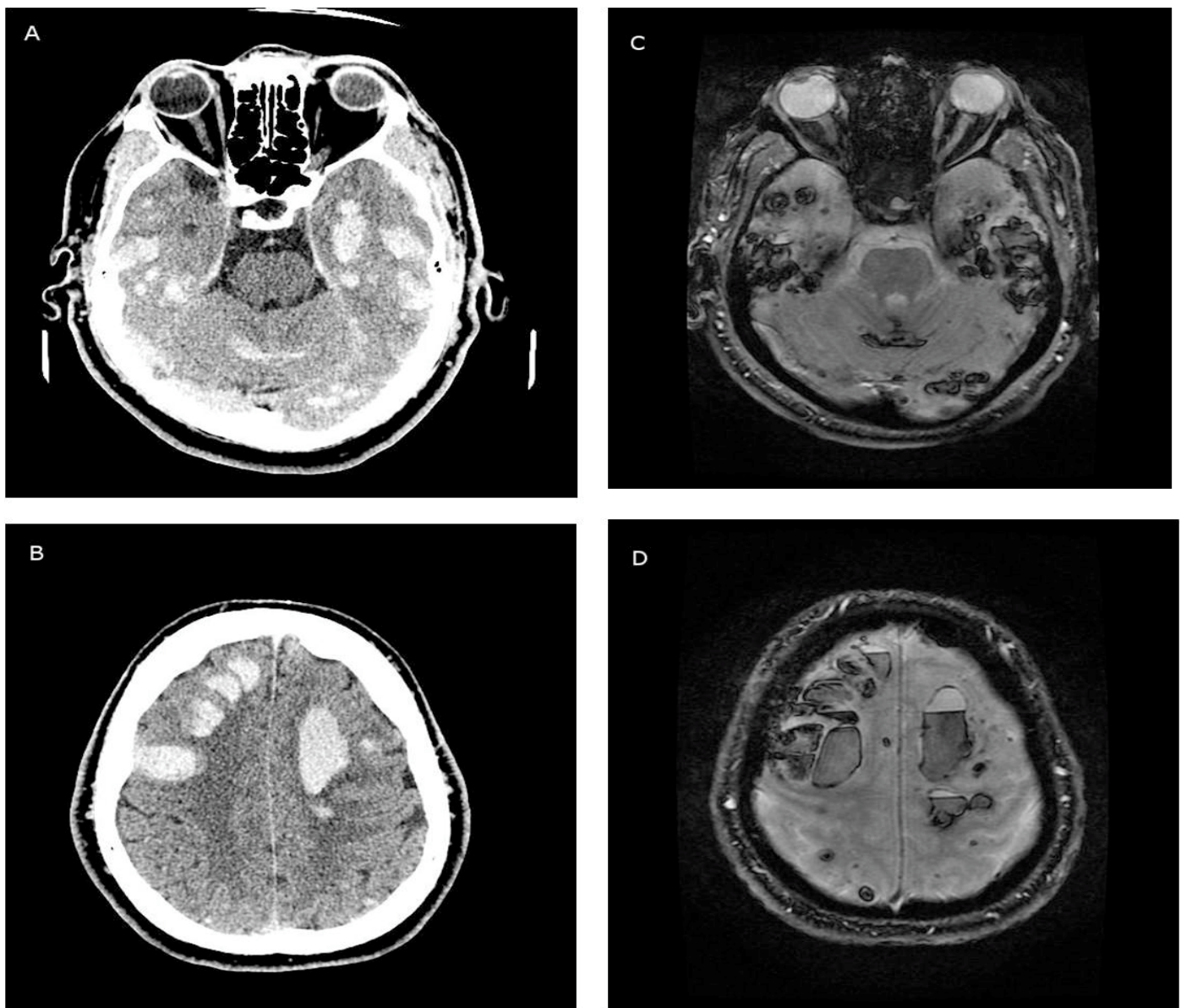


Figure 1: Panel 1A, 1B CT scan: numerous bilateral intracerebral hemorrhages. Figure 1C, 1D MRI gradient echo: intraparenchymal hemorrhages involving cerebral hemispheres and cerebellar vermis. The areas of hemorrhage are mixed signal intensity and demonstrate fluid levels. No enhancing lesions were seen.

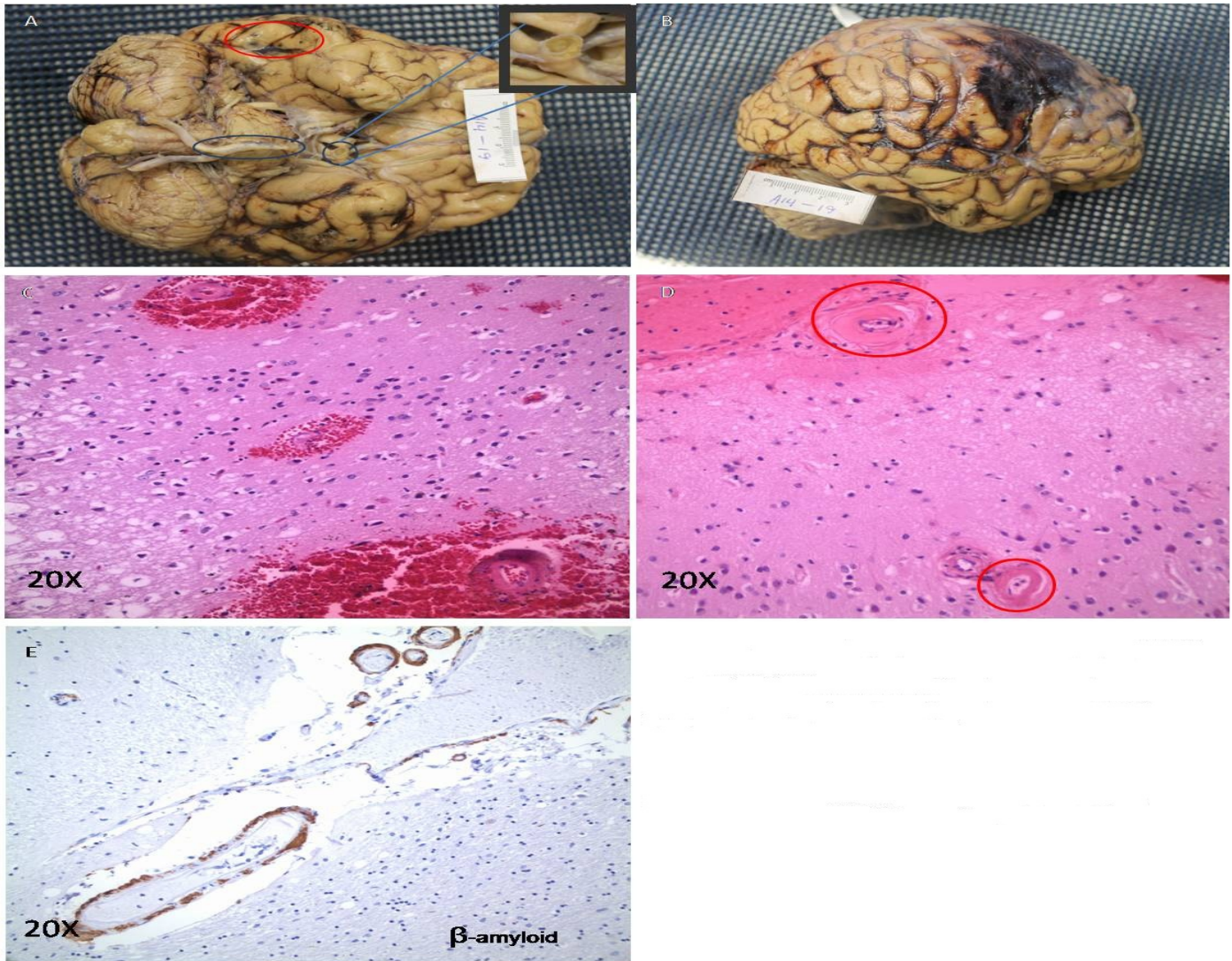


Figure 2: Amyloid angiopathy. (A) multiple punctate cortical hemorrhages were present on the brain surface (red), as well as cerebral arteriosclerosis involving the ACA and basilar artery (blue). (B) Large hemorrhagic infarct on frontal lobe. (C,D) H&E stain shows thickened hyalinized amorphous deposits within the vessel walls leading to vessel fragility and bleeding. (E) monoclonal Ab against β -amyloid highlights presence on the protein.

Discussion/Conclusion

Currently, tPA is the standard of care for acute ischemic stroke in patient presenting within 4.5 hours from symptom onset. Neither a history of dementia, nor the radiologic manifestation of amyloid angiopathy is currently a contraindication to tPA therapy although cases of post-tPA hemorrhages in patients with amyloid angiopathy have been described [5]. Notably, MRI is the required imaging modality to identify micro-bleeds, but this is not routinely performed before thrombolytic administration. Better understanding of the epidemiological and radiological manifestations of amyloid angiopathy and its role in the risk of post-tPA hemorrhage is needed. This might help physicians to identify patients at higher risk for post-tPA hemorrhage, prompting emergent MRI in a selected population without delaying best medical care.

In addition, future studies are needed to provide better insight about relation of post thrombolysis PHr and amyloid angiopathy. Besides, PHr findings on post tPA imaging may serve as a predictor for the underlying amyloid angiopathy and prompt physicians for thorough investigation.

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