Status epilepticus in cerebral amyloid angiopathy-related inflammation: a case series

F. Rossato[1], L. Pellegrino[1], A. Petullà[1], N. Ravì[1], R. Ragone[1], F. Dainese[2] , M. Corbetta[1], A. Cagnin[1,*]

1 Neurology Unit, 2 Clinical Neurophysiology , Department of Neuroscience - University of Padova, * ICAB and SINdem CAA Study Group

Introduction and aim

Cerebral amyloid angiopathy-related inflammation (CAA-ri) is characterized by an anti-amyloid immune response towards cerebrovascular-deposited amyloid-beta protein. Clinically, the relapsing-remitting condition may present with acute focal neurological signs, epilepsy and cognitive impairment.
We characterize incidence, type and response to treatments of status epilepticus (SE) in a cohort of CAA-ri patients.

Methods

This is a case series derived from a single centre longitudinal cohort of 30 CAA-ri patients enrolled from 2012 to 2024 at Padova Neurology Unit. Frequency of SE was collected and demographic, clinical, EEGraphic, brain MRI, CSF biomarkers features of patients with SE were described along with drug treatment response and outcomes.

Case series

Patient ID	CAAri	CSF protein (g/L)	CSF WBC (cell/uL)	CSF ATN	ApoE	EEG	MRI	ASM	Immune therapy	Outcome
1	Onset	0,27	1	A+T+N+	E3/E3	IIC (R>L)	R F-P oedema + MBs + cSS	LEV → BRV, LCM, VPA, PER	MPS 5 days + tapering	Death
2	Onset	0,26	0	X	E3/E3	IIC(R>L)	R oedema + MBs + cSS	LEV → BRV, LCM, VPA, PER, Keto diet	MPS 5 days + tapering	Survival with epilepsy
3	Onset	0,32	0	A+T-N+	E3/E3	R T-P spike and waves	R F-P oedema	LEV, LCM, PER	MPS 6 days + tapering	Death
4	Onset	1,23	122	A+T-N+	E3/E4	R T sharp waves	R F-P oedema + sulcal hyperintensities	BDZ, LCM, PHT, VPA	MPS 9 days + tapering	Death
5	Relapse	0,61	13	A+T+N-	E3/E4	R F-T spike and waves	R P oedema near chronic ICH	BDZ, VPA	MPS 3 days + tapering	Survival with epilepsy
6	Relapse	0,35	6	A+T+N+	E3/E3	L T-P spikes	L P oedema	VPA	no	Survival with epilepsy

Table 1: biomarker, EEG, MRI, therapy and outcome variables.
ASM anti seizure medication, ATN amyloid/p-tau/tau, cSS cortical siderosis, F frontal, ICH intracranic haemorrhage, IIC ictal-interictal continuum, L left, MB microbleed, MPS methylprednisolone P parietal, R right, T temporal

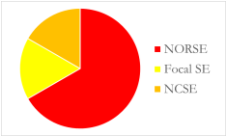

Figure 1: clinical-EEG presentation

Six out of 30 CAA-ri patients were diagnosed with SE: mean age was 76 ± 7.6 years, 5/6 (83%) were female, 1/6 had cognitive impairment. No patient had previous seizures or history of epilepsy.

In 4 cases (67%) SE was among presenting symptoms of CAA-ri. In these cases, SE had brief focal motor semiology and rapidly evolved in new onset (NORSE) super-refractory type.
In the other 2 cases (33%), SE manifested during a CAA-ri clinical relapse: 1 focal motor SE five months after an untreated first episode of CAA-ri and 1 non convulsive SE (NCSE) ten months after the onset of CAA-ri successfully treated with metilprednisolone boluses and prednisone tapering in 3 months.

Intercritical EEG showed ictal-interictal continuum in 2 patients and focal epileptiform discharges in 4.
CSF analysis showed CSF inflammation in 1/4 cases (with high Qalb and IgG index) and altered ATN biomarkers in 3/4 de novo SE patients, while in both relapsing patients showed CSF pleiocytosis (with 1/2 high Qalb) and altered ATN profile.
Brain MRI excluded acute lobar and subarachnoid haemorrhage with findings suggestive of CAA-ri (4 de novo lobar oedema, 2 new onset oedema near chronic haemorrhagic lesions).

Despite treatment with 1 to 6 antiseizure drugs (apart from sedatives) and high dose steroid therapy with tapering, 4 patients needed ICU admission. SE mean duration was 23 ± 15 days with a global mortality of 50%. Survivors needed long term antiseizure therapy.

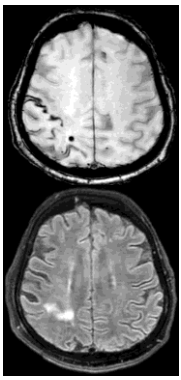

Figure 2: SWI (top) and FLAIR (bottom) MRI sequences with evidence of cSS, MBs, white matter hyperintensities

Discussion

CAA-ri is a cause of severe SE and NORSE, with significant mortality ang long-lasting epilepsy in survivors. Cortical siderosis and sulcal hyperintensities are associated with SE. CAA-ri must be considered in the differential diagnosis of SE, particularly in older patients, with cognitive impairment or previous intracerebral haemorrhages. Its recognition should prompt immunomodulant therapy.

Contact: francesco.rossato@aopd.veneto.it