

Early postmortem brain MRI findings in COVID-19 non-survivors

*Tim Coolen, MD**; *Valentina Lolli, MD**; *Niloufar Sadeghi, MD, PhD*; *Antonin Rovai, PhD*;
Nicola Trotta, PhD; *Fabio Silvio Taccone, MD, PhD*; *Jacques Creteur, MD, PhD*; *Sophie
Henrard, MD*; *Jean-Christophe Goffard, MD, PhD*; *Olivier Dewitte, MD, PhD*;
Gilles Naeije, MD, PhD; *Serge Goldman, MD, PhD*; *Xavier De Tiège, MD, PhD*

Supplemental Data

Table e-1

**This table is too large to be displayed on one page.
It is therefore spread on 4 successive pages.**

D	Symptoms at presentation						Temperature		Confirmatory tests		Treatment		
	Dyspnea	Cough	Neurological	GI	RR	SaO2	Admission	Death	Nose Swab	Chest CT	Anticoagulation	ICU	ECMO
D1	1	1	0	0	34	74	38.3	37	rtPCR +	20	Prophylactic	0	0
D2	1	1	Headache	0	30	79	40.6	N/A	rtPCR +	15*	Therapeutic	1	1
D3	1	0	0	Vomiting	25	76	38	36.6	rtPCR +	11	Therapeutic	0	0
D4	1	0	Agitation	0	25	79	35.6	39	rtPCR +	18	Prophylactic	0	0
D5	1	1	Confusion	0	20	74	37	36.7	rtPCR +	>12**	Prophylactic	0	0
D6	1	0	One seizure before admission	0	23	94	37.8	37.5	rtPCR +	11	Prophylactic	0	0
D7	1	0	0	0	23	89	36.9	36.6	rtPCR +	16	Prophylactic	0	0
D8	1	1	0	Diarrhea	38	88	39.1	37.7	rtPCR +	25	Therapeutic	1	1
D9	1	1	Headache	0	35	64	38.8	34.8	rtPCR +	21	Therapeutic	1	1
D10	0	0	Confusion	0	18	93	36.2	36.3	rtPCR +	Abnormal CT**	Prophylactic	0	0
D11	1	1	Confusion	0	22	94	38.1	36.6	rtPCR +	17	Prophylactic	0	0
D12	1	1	0	0	23	88	36.2	36.1	rtPCR +	Abnormal CT**	Prophylactic	0	0
D13	1	0	0	Diarrhea	38	90	38.8	39.5	rtPCR +	9	Prophylactic	0	0
D14	1	0	0	0	18	85	36.4	36.7	rtPCR +	23	Prophylactic	0	0
D15	1	1	N/A	Diarrhea	25	82	N/A	N/A	rtPCR + (BAL)	21	Prophylactic	1	0
D16	1	0	Confusion	0	22	95	36.8	38.1	Ag +	3	Therapeutic	0	0
D17	1	1	0	1	20	75	36.3	36.5	rtPCR +	16	Prophylactic	0	0
D18	1	1	0	0	23	92	41	35.5	Ag +	8	Prophylactic	0	0
D19	1	0	0	0	35	82	37.3	N/A	rtPCR +	19	Therapeutic	1	0

Units

rate/min % °C

score /25

* score /15 (2 lobectomies)

** Chest CT done at another institution

Ag: SARS-Cov-2 antigen

BAL: bronchoalveolar lavage

Chest CT: CT score based on Pan et al. (2020)

ECMO: extracorporeal membrane oxygenation

GI: gastrointestinal

ICU: intensive care unit hospitalization

N/A: not available

RR: respiratory rate

rtPCR: reverse-transcriptase polymerase chain reaction

SaO2: oxygen saturation

D	D-dimers		PLT		WBC		Neutro		Lympho		CRP		PCT		GFR		ALT		AST		LDH		CK		hs-Trop		Alb	
	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D	A	D
D1			350		9.9		7.11		1.39		230		0.3		38		18		57		618		261		29			
D2	755	19008	200	84	6.52	22.6	5.39	20.81	0.82	1.61	180	110	0.21	46.47	81	10	45	2542	37	7084	393	8995	84	19993	11	394	41	21
D3			347	406	11.3	21.6	9.67	19.39	0.44	0.99	270		1.87	23.18	58	39	22	29	57	104	359	538	562	973	55	209	29	25
D4			390		11.6		10.55		0.68		100		0.46		31		23		40		710		237		29		27	
D5			290	278	16.4	26	14.42	19.35	0.33		270	230	0.44		33	31	14	12	32	26	404	402	195		60		25	
D6	3088		209	256	16.1	9.1	13.95	7.4	0.73	0.6	270	340	2.46	1.35	10	5	29	56	115	182	335	475	5044	6790	157	150	38	31
D7			169	202	4.9	20.3	4	18.94	0.57	0.9	200	380	>100		22	19	68	30	78	24	542	360	360	73	59		34	28
D8	>35000	12521	258	506	14.7	36.1	10.73	24.19	0.97	3.29	270	160	7.4	9.13	22	6	28	52	106	82	802	836	1302	94	26	157	19	23
D9	1628	2622	200	183	8.69	19.9	7.73	20.39	0.7	4.67	170	94	1.01	4.31	18	6	24	836	43	1295	563	2930	118	316	20	51	36	18
D10			172	413	18.6	12	11.6	6.53	0.93	1.86	160	25			35	43	20	22	24	22	185	219	101	178		368	37	30
D11		>35000	152	192	5.8	11.3	5.9	10.63	1.29	0.27	71	250	0.18	1.86	61	48	29	18	39	20	232	432	80	38	22	50	33	25
D12			334	337	4.9	7.06	3.45	6.23	0.67	0.58	40	100	0.48		84	93	12	13	26	41	368	505	100	358	22		29	
D13	1390		259	276	8.52	9.69	7.19	8.13	0.55	1.27	100	280	2.06	4.25	15	13	11	12	40	35	281	254	127	124	184	186	30	26
D14	>35000		302	429	12.6	19.8	11.77	16.13	0.41	0.93	170	220	1.11		55	32	35	29	157	190	488	973	1095	4112	48	81	29	
D15	27467	10053	271	229	9.12	15	8.21	10.47	0.66	1.62	78	190	4.89	16.2	44	29	18	520	33	1069	576	1414	351	1501	39	96	31	21
D16			63	82	16.7	7.3	13.64	6.53	0.61	0.26	450	320	1.8		11	7	10	10	26	43	291	277	161	135	30	34	25	26
D17		2590	252	114	10.2	11	6.25	10.47	1.21	0.33	17	360	17	73.73	57	49	21	173	33	320	165	832		95		281	24	29
D18		1053	159	46	2.16	1.12	1.33	1.24	0.53	0.08	56	230	0.86	10.37	45	87	30	54	24	61	289	283	80		114		40	
D19	10748	4268	402	377	16.8	11.8	14.26	8.47	1.37	0.96	230	490	0.82		95	16	77	16	213	31	787	443	11826	322	15	92	34	18

Units	ng/ml	x10 ³ /mm ³	x10 ³ /mm ³	x10 ³ /mm ³	x10 ³ /mm ³	mg/L	µg/L	mL/min/1.73 m ²	U/L	U/L	U/L	U/L	ng/L	g/L
	NV:<500	NV:150-440	NV:3.5-11	NV:1.5-6.7	NV:1.2-3.5	NV:<5.0	NV:> 0.25	NV:>60	NV:<33	NV:<32	NV:135-214	NV:26-192	NV:<14	NV:40-49

A: earliest value, closest to admission

Alb: albumine

ALT: alanine transaminase

AST: aspartate transaminase

CK: creatine kinase

CRP: C-reactive protein

D: latest value, closest to death

GFR: glomerular filtration rate

hs-Trop: high-sensitivity troponin T

LDH: lactate dehydrogenase

Lympho: lymphocytes

Neutro: neutrophils

NV: normal values

PCT: procalcitonin

PLT: platelets

WBC: white blood cells

D	Complications						Admission to death	MRI scan delay after death	
	Respiratory failure	Coagulopathy	Shock	Acute Kidney Injury	Acute Cardiac Injury	Neurological			Cause of death
D1	1	0	0	1	1	0	Refractory Respiratory Failure	2	20.13
D2	1	1	1	1	1	0	Septic Shock / MOF	10	22.37
D3	1	1	0	1	1	0	Refractory Respiratory Failure	1	17.82
D4	1	1	0	1	1	1	Refractory Respiratory Failure	1	2.07
D5	1	0	0	0	1	1	Refractory Respiratory Failure	6	2.80
D6	1	0	0	1	1	0	Refractory Respiratory Failure	4	3.52
D7	1	0	0	0	1	1	Refractory Respiratory Failure	7	5.05
D8	1	0	1	1	1	0	Refractory Respiratory Failure	13	19.82
D9	1	1	1	1	1	1	Septic Shock / MOF	10	17.10
D10	1	0	0	1	1	0	Refractory Respiratory Failure	21	18.75
D11	1	0	0	1	1	0	Refractory Respiratory Failure	8	3.38
D12	1	0	0	0	1	0	Refractory Respiratory Failure	4	14.90
D13	1	0	0	0	1	0	Refractory Respiratory Failure	4	12.28
D14	1	0	0	1	1	0	Refractory Respiratory Failure	2	16.77
D15	1	1	1	1	1	0	Septic Shock / MOF	33	4.35
D16	1	0	0	1	1	0	Refractory Respiratory Failure	16	23.75
D17	1	0	0	1	1	0	Refractory Respiratory Failure	2	21.00
D18	1	0	0	0	0	0	Refractory Respiratory Failure	28	15.42
D19	1	1	1	1	1	1	Septic Shock / MOF	20	18.4

Units

days

hours

MOF: multiple organ failure

	Scan delay (h)	FLAIR TI (ms)	Increased T1WI SI					T2WI FS	DWI	ADC values (x10 ⁻⁶ /mm ²)			SWI Vessels
			P	T	SN	RN	DN			CSO	BG	CBLM	
D1	20.13	2041	2	0	2	1	0	2	2	269	392	192	3
D2	22.37	1706	2	2	2	2	2	2	2	248	428	223	0
D3	17.82	1702	2	0	2	2	0	2	2	220	276	251	1
D4	2.07	1972	1	1	1	2	0	1	1	296	420	382	2
D5	2.80	1967	1	0	1	1	0	1	2	253	297	329	2
D6	3.52	1971	0	0	1	1	0	1	1	271	356	303	1
D7	5.05	1960	0	0	1	1	0	1	1	277	468	318	1
D8	19.82	1961	2	1	2	2	2	2	2	214	228	218	1
D9	17.10	1704	2	1	2	2	1	2	2	222	264	250	0
D10	18.75	1432	1	1	2	1	1	2	2	152	216	174	0
D11	3.38	2033	0	0	0	0	0	1	1	320	503	417	2
D12	14.90	1430	2	1	2	2	2	2	2	207	245	184	1
D13	12.28	1682	1	0	1	1	0	1	2	186	260	166	1
D14	16.77	1703	2	1	2	2	0	2	2	238	320	191	1
D15	4.35	2041	1	0	1	1	0	2	2	347	502	434	2
D16	23.75	1333	2	0	2	2	2	2	2	228	236	174	1
D17	21.00	1431	2	0	1	1	1	2	2	152	220	152	1
D18	15.42	1631	1	1	1	1	1	2	2	197	243	205	1
D19	18.40	1545	2	1	2	2	2	2	2	200	350	176	2
Spearman's rho	-.67		.68 (sum of 5 items)					.76	.61	-.57 (sum of 3 items)			-.42
p-value	.0032**		.0015**					.0001**	.0053**	.0128*			.0766

Table e-2: Postmortem changes. Decedent number is shown in the first column (D1, ..., D19). The second column indicates the delay between death and MRI data acquisition. The third column indicates the time of inversion (TI) of the T2WI FLAIR sequence that was adapted in each decedent in order to obtain adequate CSF signal suppression. The increase of T1WI signal intensity was categorized as absent (0), mild (1), or marked (2) and reported in columns 4-8 in the bilateral pallidi (P), postero-lateral thalami (T), substantia nigra (SN), red nuclei (RN) and dentate nuclei (DN).

Assessment of fat suppression on T2WI (T2WI FS, column 9) as well as the cortical and periventricular rim of increased SI on DWI (column 10) were classified as incomplete (1) or complete (2). ADC values are reported in left centrum semiovale (CSO), left basal ganglia (BG) and left cerebellum (CBLM) in columns 11-13. The increase of vessels visibility on SWI (SWI vessels) was classified as absent (0), discrete (1), moderate (2), or marked (3) and detailed in the rightmost column. The last two separate rows detail the Spearman's rank correlation *rho* coefficients, indicating the direction and strength of the relationship between scan delay and the evaluated parameters along with their *p*-values. For the increased T1WI signal intensity and the ADC values, the sum of the items in that category was used for the computation. Significant ($p < .05$) results are indicated by an asterisk (*) and those surviving Bonferroni multiple comparison correction ($n=6$) are marked by a double asterisk (**).

	Recent antemortem changes	Olfactory Bulb Asymmetry	Olfactory Cleft Obliteration	Long-standing antemortem changes				
				WMC	EPVS	Ischemic or hemorrhagic sequelae	Atrophy	
							GCA	EI
D1	None	None	None	3	2	R centrum semiovale and L cerebellar lacunes; R temporal microbleed	1	0.30
D2	Disseminated supra- and infratentorial micro- and macro- subcortical hemorrhages	None	Bilateral*	0	0	None	0	0.28
D3	None	None	None	2	2	L thalamic lacune	2	0.32
D4	R subcortical occipito-temporal macro-hemorrhages	None	None	1	0	L thalamic lacune	3	0.31
D5	None	R>L	None	2	0	R cerebellar lacune; L cerebellar microbleed	1	0.27
D6	None	None	None	1	2	R temporoparietal cortical sequelae; R cerebellar microlacune	1	0.32
D7	Bilateral parietal cortical and paracentral subcortical edema	None	None	3	0	None	1	0.33
D8	None	L>R	L*	0	2	None	0	0.27
D9	Extensive hazy increased T2WI SI of centrum semiovale white matter	None	Bilateral*	0	4	None	0	0.23
D10	None	None	L*	2	2	None	2	0.33
D11	None	L>R	None	2	4	None	2	0.33
D12	None	L>R	None	3	2	None	1	0.24
D13	None	None	None	1	0	None	2	0.32
D14	None	None	None	1	2	None	2	0.35
D15	None	None	Bilateral*	1	2	None	0	0.26
D16	None	None	None	1	2	None	1	0.30
D17	None	None	None	2	0	None	1	0.31
D18	None	None	None	1	2	L cerebellar lacune	0	0.25
D19	None	None	Bilateral*	1	2	L periventricular lacune	1	0.26

Table e-3: Signal abnormalities of presumed antemortem origin. Decedent number is shown in the first column (D1, ... D19). Recent changes are described in the second column. Olfactory bulb asymmetry is detailed in the third column with, e.g., R>L denoting a relatively larger right (R) bulb compared to the left (L). Olfactory cleft obliteration is listed in the fourth column and can be left-sided (L), right-sided (R) or bilateral and may be associated with other naso-sinusal mucosal thickening (*). Chronic changes are detailed in columns 5-9. White matter changes (WMC) were graded from 0 to 3 according to the Fazekas scale and detailed in the fifth column. The sixth column describes the enlargement of perivascular spaces (EPVS), which was graded from 0 to 8. Ischemic or hemorrhagic sequelae were described when present in the seventh column. Cerebral atrophy was rated by retaining the highest Global Cortical Atrophy (GCA) score ranging from 0 to 3 (eighth column) and by calculating the Evan's index (EI) for each patient (ninth column).



Figure e-1: Small mid-pontine ill-defined T2 and T2 WI FLAIR signal abnormality in D10. Superior and midline pontine centimetric T2 high signal abnormality probably corresponding to a capillary telangiectasia (Left, Axial T2 WI; Middle, Sagittal T2 WI FLAIR; Right, Reformatted sagittal SWI).

In D10, the isolated superior pontine T2WI hyperintense lesion is evocative of a capillary telangiectasia. Still, the absence of low intralesional signal intensity on SWI (along with the impossibility to inject contrast medium) leaves some doubt concerning this etiology.³¹ This finding could also represent early central pontine myelinolysis.³² Typical MRI findings of central pontine myelinolysis include edema centrally within the pons sparing the cortico-spinal tracts, however with a characteristic symmetric trident pattern which was not observed.³² Furthermore, the decedents' clinical history does not support this diagnosis (no important hyponatremia). Moreover, involvement of the pons has also been rarely

described in viral encephalitis.³³ Nonetheless, brainstem lesions in the course of encephalitis are commonly associated with supra-tentorial signal abnormalities, often showing symmetric and bilateral involvement of the basal ganglia.³⁴ These other hypotheses are therefore unlikely. Further MRI studies in larger cohorts are needed to definitely exclude signs of SARS-CoV-2 brainstem lesions.