

1 **Supplementary Table 1: Baseline characteristics of children with acute**
2 **necrotizing encephalopathy in low- and high-dose groups.**

	Low-dose	High-dose	
	group	group	
Variables	(<i>n</i> = 25)	(<i>n</i> = 11)	<i>P</i> value
Basic information			
Age (years)	2.5 (1.4, 4.6)	3.0 (2.1, 3.8)	0.810
Gender (male)	11 (44.0)	5 (45.5)	1.000
Season of onset (winter)	14 (56.0)	7 (63.6)	0.729
Underlying disease	1 (4.0)	0	1.000
Family history of encephalopathy	1 (4.0)	0	1.000
Duration from consciousness disturbance	24 (10, 72)	24 (10, 48)	0.677
to admission (h)			
Clinical features			
Fever	25 (100)	11 (100)	NA
Convulsion	24 (96.0)	11 (100)	1.000
Consciousness disturbance	25 (100)	11 (100)	NA
Shock	12 (48.0)	2 (18.2)	0.142
GCS score on admission	6 (3, 7)	6 (6, 8)	0.112
ANE severity score on admission (low	15/10	7/4	1.000
and medium risk vs. high risk)*			

3 Data are shown in median (P_{25} , P_{75}) or *n* (%). *Lumbar puncture was not conducted in
4 four patients, but the pathogen underlying the prodromal infection was influenza virus
5 in all four patients. ANE severity score of these four patients was five to eight without
6 the routine CSF results. ANE: Acute necrotizing encephalopathy; CSF: Cerebrospinal
7 fluid; GCS: Glasgow Coma Scale; NA: Not applicable.

8 **Supplementary Table 2: Laboratory findings, treatments and outcomes for ANE**
9 **of childhood in low- and high-dose groups.**

	Low-dose group (n = 25)	High-dose group (n = 11)	P value
Variables			
Laboratory findings on admission			
Serum CRP (mg/L)	19.0 (9.5, 34.5)	8.0 (8.0, 24.0)	0.017
Serum PCT (ng/mL)	17.3 (2.6, 50.0)	12.0 (1.0, 35.9)	0.371
White blood cell count ($\times 10^9/L$)	6.4 (3.9, 10.2)	5.6 (3.5, 7.3)	0.400
Neutrophil count ($\times 10^9/L$)	4.9 (3.0, 8.4)	3.3 (2.6, 6.1)	0.216
Platelet count ($\times 10^9/L$)	131.0 (79.0, 175.5)	125.0 (87.0, 179.0)	0.718
Blood ammonia ($\mu\text{mol/L}$)	47 (28, 59)	37 (33, 49.5)	0.638
Alanine aminotransferase (U/L)	133.4 (30.0, 433.4)	63.9 (30.0, 591.0)	0.823
Aspartate aminotransaminase (U/L)	204.0 (58.9, 1145.4)	137.2 (74.0, 960.4)	0.904
CSF cell count ($\times 10^6/L$)*	2.0 (1.5, 4.0)	1.5 (0, 4.8)	0.213
CSF protein (mg/L)*	901.0 (355.5, 4080.5)	603.5 (214.5, 6319.8)	0.499
Pathogen			
Positive	16 (64.0)	7 (63.6)	1.000
Influenza/others	12/4	7/0	0.273
Cranial imaging			
Bilateral thalamus	25 (100)	11 (100)	NA
Brainstem	13 (52.0)	6 (54.5)	1.000
Treatments			
Duration of initial dose of methylprednisolone (days)	3 (1.5, 5)	3 (2,3)	0.598
Mechanical ventilation	22 (88.0)	7 (63.6)	0.167
Duration of mechanical ventilation	48.0 (10.0,	30.0 (0, 71.0)	0.248

(h)	130.5)		
Antiviral therapy	24 (96.0)	10 (90.9)	0.524
IVIG	23 (92.0)	10 (90.9)	1.000
Plasma exchange	7 (28.0)	5 (45.5)	0.446
Primary outcome			
Died at discharge	12 (48.0)	1 (9.1)	0.031
Secondary outcomes			
Length of PICU stay (days)	3.0 (1.1, 13.9)	3.1 (1.3, 11.5)	0.945
Length of hospital stay (days)	4.0 (1.5, 17.4)	13.0 (2.0, 25.0)	0.388

10 Data are shown in median (P_{25} , P_{75}) or n (%). *Lumbar puncture was not conducted in
11 four patients (three patients in the low-dose group and one in the high-dose group).
12 ANE: Acute necrotizing encephalopathy; CRP: C-reactive protein; CSF:
13 Cerebrospinal fluid; IVIG: Intravenous immunoglobulin; NA: Not applicable; PCT:
14 Procalcitonin; PICU: Pediatric intensive care unit.

15 **Supplementary Table 3: Differences in indicators between admission and 3 days**
16 **after treatment in the low- and high-dose groups.**

Variables	Low-dose group			<i>P</i>	High-dose group			<i>P</i>
	<i>(n = 13)</i>				<i>(n = 7)</i>			
	At admission	3 days after treatment			At admission	3 days after treatment		
C-reaction protein (mg/L)	26.0 (10.6, 49.0)	5.0 (2.8, 8.0)	0.023	8.0 (8.0, 24.0)	8.0 (8.0, 11.0)	0.273		
PCT (ng/mL)	9.8 (4.5, 100.0)	7.7 (1.1, 38.8)	0.131	3.0 (0.2, 28.2)	1.6 (0.3, 6.3)	0.138		
White blood cell	7.1 (3.5, 10.4)	4.4 (3.2, 7.6)	0.213	4.4 (3.4, 7.3)	7.6 (5.8, 12.3)	0.128		

count						
($\times 10^9/L$)						
Neutrophil	5.5 (2.7,	2.9 (1.5, 4.8)	0.055	2.9 (2.5,	5.0 (3.5, 9.1)	0.128
count	8.4)			6.1)		
($\times 10^9/L$)						

17 Data are shown in median (P_{25} , P_{75}). PCT: Procalcitonin.

18 **Supplementary Table 4: Follow-up of children with ANE in December 2020.**

Patients who survived	Follow-up period (months)	PCPC score	POPC score
Low-dose group			
Patient 1	2	4	4
Patient 2	10	4	4
Patient 3	42	1	1
Patient 4	42	2	2
Patient 5	48	3	3
Patient 6	60	2	2
High-dose group			
Patient 7	2	3	3
Patient 8	18	1	1
Patient 9	24	1	1
Patient 10	24	4	4
Patient 11	30	3	3
Patient 12	30	3	3

19 ANE: Acute necrotizing encephalopathy; PCPC: Pediatric Cerebral Performance

20 Category scale; POPC: Pediatric Overall Performance Category scale.

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