

Supplementary table 3 Clinical characteristics of patients in our cohort

Case	Gender	Birth weight (g)	Age at onset (years)	Obesity			Hyperphagia	Age at onset (years)	Cardiorespiratory arrest	Hypoventilation			Current therapy
				Age at first visit (years)	Weight gain for one year (kg)	BMI Z scores				Polysomnography	Night	Day	
1	Male	3600	3.50	9.25	5.00	3.95	Yes	9.00	No	Central hypoventilation	Yes	No	Non-invasive ventilator
2	Female	4000	6.00	7.25	22.50	4.41	Yes	7.00	No	OSAS	Yes	No	Non-invasive ventilator
3	Male	3800	2.50	12.08	4.00-9.00	2.22	Yes	3.00	No	NA	Yes	Yes	Nasal catheter
4	Female	3200	1.83	2.33	13.00	4.53	Yes	2.33	Yes	NA	Yes	No	Give up
5	Male	3200	3.00	5.33	5.00	3.57	Yes	5.17	No	NA	Yes	No	Non-invasive ventilator
6	Male	3600	1.67	3.67	6.50	6.15	Yes	3.42	No	Central hypoventilation	Yes	No	Non-invasive ventilator
7	Female	3000	3.00	7.25	4.00	2.62	No	Not applicable	No	No	No	No	No
8	Male	3600	2.08	2.58	6.00*	5.32	Yes	3.67	No	OSAS	Yes	Yes	Nasal catheter
9	Male	3450	7.92	9.25	6.50^	3.35	Yes	9.25	No	OSAS	Yes	No	Nasal catheter

10	Female	3750	5.00	9.00	3.00	3.02	Yes	9.00	No	Central hypoventilation	Yes	No	Nasal catheter
11	Female	3750	4.00	6.92	4.00	4.04	Yes	6.92	No	OSAS	Yes	No	Nasal catheter
12	Male	2900	7.75	8.42	8.50 [#]	2.43	Yes	8.00	No	OSAS	Yes	Yes	Non-invasive ventilator
13	Female	3000	3.42	4.17	9.00 ^{\$}	6.95	Yes	3.92	Yes	OSAS	No	Yes	Non-invasive ventilator
14	Male	3150	3.17	9.92	10.00	2.88	Yes	4.17	No	OSAS	Yes	Yes	Non-invasive ventilator
15	Female	NA	3.00	5.92	10.00	7.94	Yes	5.92	No	OSAS	Yes	No	Nasal catheter
16	Female	3000	2.00	5.75	3.20	4.26	Yes	2.83	Yes	OSAS Central hypoventilation	Yes	No	Not comply with non-invasive ventilator
Sum up	M:F=8:8	-	3.17 (1.67, 7.92)	7.25 (2.33, 12.08)	(3.00-22.5) kg per year	4.23± 1.65	15:1	5.55 (3.61, 8.25)	3:13	OSAS: 69.2%; Central hypoventilation: 30.8%	15:1	5:11	Non-invasive ventilator: nasal catheter=9:6

Hypothalamic dysfunction										
Case	Age at onset (years)	Hyperprolactinemia (ng/ml)	Hypothyroidism	Low IGF-1 levels (ng/ml)	Adrenocortical insufficiency	Hypernatremia (>145mmol/L)	Hyponatremia (<135mmol/L)	Polyuria	Precocious puberty	Delayed puberty
1	9.25	No	No	No	No	149.60	No	No	No	unknown
2	6.00	No	No	No	No	No	No	Yes	No	unknown
3	3.00	No	No	42.60 (143.00-506.00)	No	148.10	123.50	No	No	Yes
4	1.83	120.89 (3.10-15.70)	Yes	No	Yes	155.10	No	Yes	No	unknown
5	5.08	43.39 (4.50-18.0)	Yes	No	No	No	No	No	No	unknown
6	3.58	No	No	No	No	No	No	Yes	No	unknown
7	6.08	26.29 (3.10-15.70)	No	34.60 (57.00-277.00)	No	159.50^	128.70	Yes	No	unknown
8	2.08	49.48 (3.60-28.60)	Yes	No	No	155.90^	121.10	No	No	unknown
9	None	No	No	No	No	No	No	No	No	unknown
10	4.00	23.28 (3.10-15.70)	No	23.10 (57.00-277.00)	No	No	No	Yes	No	unknown
11	6.92	50.07 (3.10-15.70)	Yes	No	No	No	No	Yes	No	unknown
12	8.42	No	Yes	36.10 (40.00-255.00)	No	No	109.40	No	No	unknown
13	3.50	①80.7; ②67.3; ③60.4; ④86.2 (4.80-23.30)	Yes	34.60 (40.00-255.00)	No	156.00	126.00	No	No	unknown
14	4.42	①138.00; ②156.00; ③	No	32.90	No	148.00^	No	Yes	No	unknown

		119.00 (4.80-23.30)		(40.00-255.00)							
15	4.50	113 (4.80-23.30)	No	42.10 (40.00-255.00)	No	158.80^	No	Yes	No	unknown	
16	2.50	No	No	52.40 (108.00-232.00)	No	No	No	No	No	unknown	
Sum up	4.46 (1.83, 9.25)	9:7	6:10	8:8	1:15	8:8	5:11	8:8	0:16	1:15	

Autonomic dysregulation										
Case	Age at onset (years)	Fever	Circadian rhythms and sleep	Excessive sweating	Cold hands and feet	Cardiovascular manifestations	Strabismus	Abnormal pain threshold	Gastrointestinal disturbances	Comment
1	3.50	Yes	Yes	Yes	No	Yes	Yes	No	Yes	6 symptoms
2	4.00	No	No	Yes	No	No	Yes	Yes	Yes	4 symptoms
3	2.50	No	Yes	Yes	No	Yes	No	No	Yes	4 symptoms
4	1.83	Yes	No	No	No	Yes	No	No	Yes	3 symptoms
5	5.08	Yes	No	No	No	Yes	Yes	Yes	Yes	5 symptoms
6	3.42	Yes	Yes	No	No	Yes	Yes	No	No	4 symptoms
7	2.00	No	No	Yes	Yes	Yes	Yes	No	No	4 symptoms
8	2.08	Yes	Yes	Yes	Yes	No	Yes	No	Yes	6 symptoms
9	7.92	No	Yes	Yes	No	Yes	No	No	Yes	4 symptoms
10	3.00	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	7 symptoms
11	5.50	Yes	No	No	No	Yes	Yes	No	Yes	4 symptoms
12	8.00	Yes	Yes	No	No	Yes	Yes	No	Yes	5 symptoms

13	3.50	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	7 symptoms
14	3.17	Yes	No	Yes	Yes	No	Yes	Yes	No	5 symptoms
15	3.00	No	Yes	Yes	Yes	Yes	No	No	No	4 symptoms
16	4.00	Yes	No	Yes	Yes	Yes	Yes	No	No	5 symptoms
Sum up	3.42 (1.83, 8.00)	68.8%	50.0%	68.8%	43.8%	81.2%	62.5%	25.0%	62.5%	≥ 4 symptoms 93.8%, on average, each patient has 4.8 symptoms of autonomic dysregulation

Case	Abnormal behavior	Type and location of neural tumors	Other clinical manifestations	Molecular genetics
1	Yes	Left adrenal nodule, inhomogeneous enhancement	Bilateral optic nerves were blocked	Negative (WES, trios)
2	Yes	Cervical neuroblastoma	No	ABCL1 (WES, trios)
3	Yes	None	Bilateral cryptorchidism, seizure	Negative (WES, trios)
4	No	None	Seizure, general weakness, developmental regression	NA
5	Yes	Left adrenal nodule, homogeneous enhancement	Seizure, general weakness	Negative (WES, trios)
6	Yes	None	Seizure, general weakness	Negative (WES, trios)
7	No	Left adrenal ganglioneuroblastoma	Seizure, general weakness. The right optic nerve fiber is thin	Negative (WES, patient only)
8	Yes	None	General weakness, developmental delay	Negative (WES, patient only)

9	Yes	None	Seizure, general weakness, osteoporosis	Negative (WES, tiros)
10	Yes	Retroperitoneal neuroblastoma	Seizure	NA
11	Yes	Right adrenal ganglioneuroblastoma	No	NA
12	Yes	ganglioneuroblastoma located in left paravertebral sympathetic chains	Brain atrophy, rhabdomyolysis, severe sensorineural hearing loss in both ears, bilateral eyelid drooping	Negative (WES, patient only)
13	Yes	None	serum and cerebrospinal fluid antibodies (+)	Negative (WES, tiros)
14	Yes	None	Seizure, cranial MR Abnormalities	Negative (WES, patient only)
15	Yes	Right adrenal ganglioneuroblastoma	serum and cerebrospinal fluid antibodies (+)	Negative (WES, tiros)
16	Yes	Mediastinal neural original lesions	developmental delay, Seizure, pituitary MR Abnormalities	Negative (WES, tiros)
Sum up	14:2	Ganglioneuroblastoma: 4; Neuroblastoma: 2; Adrenal nodule: 2	-	-

Note: *:6kg for half a year; ^: 6.5kg for one month; #:8.5kg for half a year; \$:9kg for 9 months; ^: These patients have reduced thirst. NA: Not available; None: No tumor.