

Supplementary table 1 Clinical signs and symptoms of ROHHAD(NET) syndrome

Categories	Diagnosis	Clinical signs or symptoms
Rapid onset obesity	Eating disorders	1) Hyperphagia: extensive hunger/food obsession, binge-eating; 2) Hypophagia: Failure to thrive
Hypoventilation	Central hypoventilation	1) Cyanotic episodes; 2) Need artificial ventilatory support after falling asleep; 3) Hypoxemia while awake; 4) Blood gas analysis suggests carbon dioxide retention; 5) OSAS
Hypothalamic dysfunction	Central precocious puberty	Boys < 9 years of age: Testicular volume $\geq$ 4ml; Girls < 8 years of age: Tanner stage B2
	GH deficiency	Decreased growth velocity/short stature and low IGF-1 level
	TSH deficiency	Fatigue, decreased growth velocity, increasing BMI
	ACTH deficiency	Hypoglycemia, prolonged fever, abdominal or head aches
	LH/FSH deficiency	Delayed or no pubertal development, micropenis and/or cryptorchidism
Autonomic dysregulation	Diabetes insipidus with/without adipsia	1) Polyuria/polydipsia; 2) Hypernatremia/hyponatremia
	Hyperprolactinemia	Prolactin levels are above the upper limit of the normal range for at least 2 times
Autonomic dysregulation	Sleep disorder	1) Hypersomnia: daytime sleepiness or falling asleep at random places during the day; 2) Insomnia: difficult falling asleep, frequently wake at night, or screaming during asleep; 3) Sleep-wake abnormalities: Wake up extreme early, almost never sleep in, or go to bed extreme early; 4) Sleep apnea: Snoring, fatigue; 5) Multiple sleep latency test(MSLT) is positive or the patient is diagnosed with narcolepsy

Temperature regulation disorders	1) Hypothermia: cold hands and feet, temperature < 36°C; 2) Hyperthermia: warm hands and feet, temperature > 37.3°C without infection, rheumatic or autoinflammatory diseases; 3) Temperature dysregulation: frequently cold or warm hands, feet and face at unusual moments
Abnormal cardiovascular system	1) Bradycardia; 2) Tachycardia; 3) Autonomic nervous system-mediated syncope (vasovagal syncope, postural tachycardia, orthostatic hypotension, orthostatic hypertension)
Abnormal gastrointestinal system (referring to long-term problems)	1) Constipation; 2) Diarrhea; 3) Longer time to defecate (without surfing the internet or other interference, it takes more than 10 minutes to defecate)
Abnormal sweating	1) Excessive sweat after falling asleep: mild: the sweat soaked area is less than 1/3 of the clothes; moderate: the sweat soaking area is greater than 1/3 of the clothes and less than 2/3 of the clothes; severe: the sweat soaks more than 2/3 of the clothes 2) No sweat
Ophthalmological problems	Late pupil response, strabismus, eyelid ptosis, optic nerve hypoplasia and etc.
Abnormal pain sensation	1) Hyperalgesia; 2) High pain threshold
Neurogenic bladder	More residual urine

Other signs and symptoms

Behavioral disorders

1) Obsession, repetition, obsessive-compulsive symptoms;  
2) Hoarding behavior (collecting unnecessary things); 3) Hallucinations; 4) Childish behavior/aggressive behavior; 5) Logic confusion, mental disorder; 6) Indifference, lack of facial expression; 7) Cognitive decline; 8) Social disorder; 9) Uncontrollable anger

Tumors of neural crest origin

1) Neck mass; 2) Tumor found by chest or abdomen imaging

Non-specific symptoms and signs

1) Neurological symptoms, like seizures or hypotonia; 2) Developmental delay or regression; 3) impaired glucose tolerance or type 2 diabetes mellitus; 4) Fatigue

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