SPINAL MUSCULAR ATROPHY (SMA) DIFFERENTIAL DIAGNOSIS

Certain signs of SMA are readily identifiable but symptoms can overlap with other common infantile neuromuscular diseases (NMDs)[1,2]

This clinical similarity, the rarity of NMDs and the wide range of differential diagnoses can combine to make a rapid and direct diagnosis difficult[3,4]

Integration of caregiver concerns, your clinical examination and the medical history can help you obtain a differential diagnosis[3–5]

HISTORY	WHAT YOU WOULD EXPECT TO FIND IN SMA
Birth and neonatal history[3]	No consistent associations[6–8]
Family history[3]	Sibling(s) with diagnosed SMA and/or parents with known carrier status for survival motor neuron 1 (*SMN1*) mutation(s)[7]
Dietary/feeding history[3]	History of difficulties with feeding and swallowing[6,8]
Timeline of motor milestone achievement[3,4]	History of delayed or lost motor milestones[6–8]
Age of symptom onset[4]	• Type 1: 0–6 months[6,7,9] • Type 2: 6–18 months[6,9]
Social and language development[3]	No consistent associations, cognition and speech development normal[6,10]

CLINICAL EXAMINATION	WHAT YOU WOULD EXPECT TO FIND IN SMA	
Tone[4]	Hypotonia[6,7,9]	
Strength[4]	**Age 0–6 months** • Symmetrical weakness that is more proximal than distal, in the limbs (more noticeable in the legs) and trunk[6–8] • Facial weakness develops later in the disease[6,7]	**Age 6–18 months** • Reduced muscle tone and strength in the legs and arms, perhaps with a history of poor muscle tone in the first few months of life[6,7]
Other motor findings[6–8]	**Age 0–6 months** • Tongue fasciculations and atrophy[6–8] • Head lag, unable to lift their head or has poor head control[6,8,12,13] • Difficulty breathing is caused by weakness of the intercostal muscles which leads to a paradoxical breathing pattern[6,7,9,13] • Weakness of respiratory muscles can lead to a weak cough[8,13]	**Age 6–18 months** • Fine tremor in the fingers or hands[8,11] • Progressive intercostal muscle weakness leads to restrictive lung disease[6,7]
Deep tendon reflexes[3]	Areflexia, absent or reduced deep tendon reflexes[6,7]	
Quality of the cry[3]	Weak cry[8]	
Skin abnormalities[3]	None[6–8]	
Internal organ abnormalities[3,4]	Not present[6–8]	
Scoliosis and joint contractures[6,8]	Develop later in patients with Type 2 (6–18 months)[6,8,9]	
Physical examination of the parents[3]	No findings, autosomal recessive inheritance[7]	

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DISORDERS TO CONSIDER IN THE DIFFERENTIAL DIAGNOSIS OF SMA[7]

	DISORDER	SIGNS COMMON WITH SMA	SIGNS DISTINCTIVE FROM SMA
AGE 0–6 MONTHS	X-linked infantile spinal muscular atrophy	Hypotonia, weakness, areflexia	Multiple congenital contractures and intrauterine fractures
	Prader-Willi syndrome	Hypotonia, swallowing difficulties	Poor respiratory effort is rare
	Myotonic dystrophy type 1	Hypotonia, muscle weakness	Marked facial weakness
	Congenital muscular dystrophy	Hypotonia, muscle weakness	Central nervous system (CNS), eye involvement and possible increased tone
	Zellweger spectrum disorder	Hypotonia	Hepatosplenomegaly and CNS involvement
	Congenital myasthenic syndromes	Hypotonia	Ophthalmoplegia, ptosis and episodic respiratory failure
	Pompe disease	Hypotonia	Cardiomegaly
AGE > 6 MONTHS	Guillain-Barré syndrome	Muscle weakness	Subacute onset and sensory involvement
	Duchenne muscular dystrophy	Muscle weakness, motor regression	Serum creatine kinase concentration >10–20x normal
	Hexosaminidase A deficiency	Lower motor neuron disease	Slow progression, progressive dystonia, spinocerebellar degeneration, cognitive/ psychiatric involvement
	Fazio-Londe syndrome	Bulbar weakness	Limited to lower cranial nerves, death in 1–5 years
	Monomelic amyotrophy	Muscle weakness	Predominantly cervical and tongue may be affected

Table adapted from Prior *et al.* 2019.[7]

YOUR EARLY REFERRAL FORMS A CRUCIAL STEP TO ACCURATE DIAGNOSIS[14,15]

REFER URGENTLY TO A PEDIATRIC NEUROLOGIST IF YOU SEE THE SIGNS[14,15]

#SIGNSOF SMA

signsofSMA.com

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