Spinal muscular atrophy SMA

Incidence 1:10000
Carrier 1:60
♂ > ♀

AR

motor neuron dis.

Lower
→ hypotonia
hyporeflexia
muscle atrophy
progressive weakness

أحيانا يكون عنده Bulbar weakness (medulla)
→ affect respiration.
↓
Resp. arrest
↓
death.

SMN
survival motor neuron.

√ growth of axon
√ arrest of apoptosis.

بيصير عنا ↓SMN

types 1 & 2 — 10% احتياطي
المشكلة هون. responsible 90% of function
* كلما كان فيه زيادة كان الـ prognosis أحسن "لأنه بعوض النقص".

∂ according to SMN2 #
↑ prognosis
↑ age of incidence.

بيموت من الـ resp. | بعاني من الـ orthopedics

Overview of spinal muscular atrophy types [1]

Type of SMA	Type 0 SMA (prenatal or congenital) الأسوأ	Type I SMA (Werdnig-Hoffmann disease) (infantile)	Type II SMA (late infantile)	Type III SMA (Kugelberg-Welander disease) (Juvenile) — walkers	Type IV SMA (adult SMA) الأحسن — walkers
Proportion of all SMA cases [2]	• < 1%	• ~ 55% — Non sitters, MC	• ~ 30% — Sitter, non walker	• ~ 15% — DDx:- ↓ Becker	• < 1%
Severity	• Very severe	• Severe	• Intermediate	• Mild	• Mild
Age of onset	• Prenatal	• 0–6 months	• 7–18 months	• > 18 months	• 10–30 years
Typical features	• Prenatal: absent or decreased fetal movements • At birth [3] ∘ Severe muscle weakness and hypotonia ∘ Respiratory failure	• Severe muscle weakness (flaccid paralysis) and infantile hypotonia (frog-leg posture) ∘ **Symmetrical** involvement of proximal muscles, mostly of the lower extremities ∘ Intercostal muscle weakness → paradoxical breathing • Upper cranial nerves are not affected. • Diminished or absent deep tendon reflexes • Severe bulbar palsy ∘ Respiratory failure ∘ Atrophy and fasciculations of the tongue (مهم — اللسان يتحرك حركة زي الدودة) ∘ Fasciculations of the fingers ∘ Weak cry and cough ∘ Inability to swallow → difficulty feeding, drooling, ↑ risk of aspiration • Recurrent hip dislocation	Intracranial thrombosis? (مش متأكد) • **Fine hand tremors** • Delayed motor milestones • Poor weight gain • Weak cough • Musculoskeletal abnormalities ∘ Joint contractures ∘ Hip dislocation ∘ Kyphosis ∘ Scoliosis	• Tremors • (+) Gower sign • Variable degree of muscle weakness • Cramps, muscle aches • Joint pain	* ما ركزنا
Motor milestones	• Typically, none are achieved	• Never sits	• Able to sit independently, but cannot stand without support	• Able to stand and walk independently	
Life expectancy	• < 6 months	• < 2 years	• Approx. 30 years	• Near **normal** life expectancy	

head control بالمرة ما بصير عندهم

Diagnosis :-

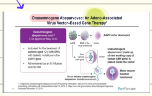
- Genetic
- EMG
  · large amplitude
  · low frequency

Treatment :-

بحسن الـ SMN2 وبحسن كفاءته وباقي أنواع الـ SMN

Nusinersen — antisense oligonucleotide. (بوزع, 1st line)
· Intrathecally ✓
· 7 doses → 1st 4 → loading —1 month→ ; then 3 → maintanec. —3 months→
· All ages
· very expensive ~3M !

Genetic
· IV
· <2 years old
· once life atime



Onasemnogene Abeparvovec: An Adeno-Associated Virus Vector–Based Gene Therapy
Onasemnogene abeparvovec-xioi
FDA approved May 2019
Indicated for the treatment of patients aged <2 y with SMA with biallelic mutations in the SMN1 gene
Administered as an IV infusion over 60 min
AAV9 vector developed
Onasemnogene abeparvovec (made up of new working copy of human SMN gene) is placed inside the vector
Vector delivers onasemnogene abeparvovec to motor neuron cell
Motor neuron function maintained
PeerView.com

Risdiplam (Risdi)
· orally
· all ages >2 months
· 60 mg / 80 mL.