**FULL PATIENTS DESCRIPTION**

**Patient #1** (video 1, Figure 1a)was a boy, the second child of healthy parents. His mother of Algerian-Tunisian origin and his father of Tunisian origin were unrelated (Fig. 1a). There was no significant family history. Spontaneous pregnancy ran without complications except a moderate right renal pyelectasis detected on the third trimester ultrasound. A premature onset of labour at 31 weeks of gestation was successfully treated by nifedipine. Patient #1 was born at 36 weeks of gestation by spontaneous vaginal delivery with normal parameters: Apgar scores 9/9/9/8, birth weight 3,460 g (76th percentile), length 50.5 cm (76th percentile), occipital frontal circumference (OFC) 34 cm (41th percentile). Respiratory distress and hypotonia occurred at 20 minutes of life requiring oxygen therapy and non-invasive ventilation (NIV). At three hours of life, the patient’s weak sucking required parenteral nutrition. The day after, physical examination revealed marked generalized stiffness, brisk tendon reflexes, truncal hypotonia, tremor of limbs, absent spontaneous movements and absent eye contact, as well as irregular and weak respiratory movements associated with a constant moaning. During the following weeks, patient #1 needed a nasogastric tube. After NIV removal, he required oxygen supply and experienced several episodes of apnea and desaturation.

Brain MRI and magnetic resonance spectrometry performed at 8 and 42 days of life were normal. EEG recordings were initially normal (days 2, 4, 11 and 21), then showed at 2 months a slow, monotone and non-reactive activity without spatial organization, amplitude and frequency were asymmetric with scarce spikes without epileptiform brain discharges. Brainstem auditory evoked responses (BEAR) were null on both ears despite stimulation up to 105 dB. PEV and ERG showed normal responses. EMG performed at 2 months of life showed a normal electromyographic activity with a permanent plastic hypercontraction. Patient #1 received a trial of clonazepam, carbamazepine and chlorpromazine without improvement. He died at 4 months of cardio-respiratory arrest.

Karyotype and array-SNP were normal. WES revealed the homozygous NM\_001321967.1:c.1070\_1071del p.(His357Argfs\*15) variant in *ATAD1* confirmed by Sanger sequencing. This variant has been previously reported in *ATAD1* encephalopathy7 with thorough functional studies and is predicted to result in a stop codon and the synthesis of a truncated protein. Analysis of the parents showed that they were heterozygous carriers.

**Patient #2** (video 2, Figure 1b)wasa boy born 5 years prior to Patient #1 to healthy consanguineous parents of French origin. His brother and other family members were healthy, except the maternal grand-mother who had epilepsy. Pregnancy ran without complications with three unremarkable ultrasounds. Patient #2 was born full term by spontaneous vaginal delivery with normal parameters: Apgar scores 10/10/10, birth weight 3,690 g (75th centile), length 49 cm (50th centile), OFC 35 cm (50th centile). Tremor, weak sucking and continuous crying were noticed during the first hours of life. Patient #2 was hospitalized because of repeated episodes of oxygen desaturation associated with limb stiffness at the tenth hour of life. Clinical examination showed generalized stiffness, truncal hypotonia, global hypomobility and brisk tendon reflexes. The child had neither eye contact nor blink reflex. He had an umbilical hernia. He needed nasogastric tube feeding, as well as oxygen therapy and intermittent NIV because of persistent hypoventilation. He underwent surgical repair of a left inguinal hernia at 2 months. Tonic seizures began when he was 3.5 months. At 5.5 months, he presented an episode of apnea with severe desaturation and bradycardia followed by generalized tonic clonic seizures. He died at the age of 6 months of a cardio-respiratory arrest.

Brain MRI and MRS (days 8 and 45, 4th month) showed a moderate left ventriculomegaly. EEG recordings were initially normal (days 3 and 29), and then showed from 3.5 months an unstable, slow background activity without organization. A tonic seizure with flattening of the activity was recorded. BAER showed no responses on both ears despite stimulation up to 105 dB. Muscle pathology, karyotype and array-SNP were normal.

WES was performed two years after the death of Patient #2 and showed several variants of unknown signification, including two compound heterozygous variants in *SCN4A* (p.Met1808Ile and p.Val1564Ile), both predicted as benign. The diagnosis was, however, not provided by this interpretation. Two years later, after the diagnosis of *ATAD1*-encephalopathy in Patient #1, we reread Patient #2’s WES data because of the similarity of their clinical presentations. This allowed the identification the homozygous Chr10(GRCh37):g.89544427C>A, NM\_001321967.1:c.383G>T, p.(Gly128Val) variant in *ATAD1* confirmed by Sanger sequencing. This variant is present on all coding refseq transcripts (NM\_001321967.1, NM\_001321968.1, NM\_001321969.1, NM\_032810.3), is absent from control databases (EVS, ExAC, gnomAD), affects a highly conserved amino-acid of the protein (GERP++ RS score 5.2) in the AAA+ ATPase domain and is considered as disease-causing with all the prediction algorithms we have tested (CADD Phred score 33, MetaSVM score 1.09, Provean Score -8.3, Revel Score 0.98). Both parents were heterozygous carriers of the variant.