Table S1. Clinical and genetic data from individuals with late-onset sulfite oxidase deficiency

Individual	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Reference	Shih VE et al., 1977	Van der Klei-Van et al., 1991	Goh et al., 1997 Pt.1	Goh et al., 1997 Pt.2	Touati et al., 2000 Pt.1	Touati et al., 2000 Pt.2	Rocha et al., 2014	Tian et al., 2019 Pt.1	Tian et al., 2019 Pt.2	Tian et al., 2019 Pt.3	Sharawat et al., 2020 Pt.1	Sharawat et al., 2020 Pt.2	Li et al., 2022	our case
General information														
Ethnicity	NA	Turkish	Chinese	Chinese	French	Turkish	NA	Chinese	Chinese	Chinese	NA	NA	Chinese	Italian
***SUOX* variant (NM_000456.3)**	NA	NA	NA	NA	NA	NA	c.[1827T>C];[827T>C]	c.[1096C>T];[1376G>A]	c.[1096C>T];[1376G>A]	c.[1096C>T];[1376G>A]	c.[1382A>T];[1382A>T]	c.[1382A>T];[1382A>T]	c.[205G>C];[1200C>G]	c.[1049_1052del];[1096C>T]
Effect on protein (NP_000447.2)	NA	NA	NA	NA	NA	NA	p.[(Leu61Pro)];[(Leu61Pro)]	p.[(Arg366Cys)];[(Arg459Gln)]	p.[(Arg366Cys)];[(Arg459Gln)]	p.[(Arg366Cys)];[(Arg459Gln)]	p.[(Asp461Val)];[(Asp461Val)]	p.[(Asp461Val)];[(Asp461Val)]	p.[(Ala69Pro)];[(Tyr400*)]	p.[(Tyr350*)];[(Arg366Cys)]
Genetic testing method	NA	NA	NA	NA	NA	NA	NA	WES	WES	WES	NGS, unspecified	NGS, unspecified	NGS, unspecified	WES
Sulfite oxidase activity in fibroblasts	absent	absent	NA	NA	absent	absent	absent	NA	NA	NA	NA	NA	NA	not performed
Sulfitest	positive	negative	NA	positive	positive	positive	positive	positive	positive	positive	positive	positive	positive	positive
Plasma homocysteine	NA	NA	NA	NA	NA	NA	0.6 mol/L (nv >4 mol/L)	3.74 µmol/L (vn 5-15 µmol/L)	3.17 µmol/L (vn 5-15 µmol/L)	2.48 µmol/L (vn 5-15 µmol/L)	0.6 µmol/L (vn 3.3–11.3 µmol/L)	1.49 µmol/L (vn 3.3–11.3 µmol/L)	1.245 µmol/L (vn 5–15 µmol/L)	<2.0 µmol/l (vn 3.7-13.9)
Gender	M	M		M	M	F	F	M	F	M	M	M	M	M
Age at onset	17 m	11 m	6 m	6 m	15 m	> 6 m	12 m	12 m	14 m	16 m	9 m	23 m	>12 m	18 m
Age at diagnosis	NA	1 y	NA	NA	22 m	9 m	4 y	9 y	5 y	4 y	NA	NA	NA	15 y
Age at last evaluation	6 y 6 m	1 y	NA	NA	4 y 6 m	3 y 2 m	5 y 1 m	9.5 y	5 y 6 m	4 y 6 m	1 y 4 m	2 y 6 m	4 y	16 y
Death	NA	NA	2 y (pneumonia)	4 y (pneumonia)	NA	NA	NA	NA	NA	NA	NA	NA	NA	alive
Family history	none	NA	yes, brother of #4	yes, sister of #3	none	yes, sister with sulfite oxydase deficiency	none	yes, minor sister (#9) and minor brother (#10)	yes, major brother (#8) and minor brother (#10)	yes, major brother (#8) and sister (#9)	none	none	none	none
Consanguineity	no	yes	no	no	no	yes	no	no	no	no	no	no	no	no
Birth														
Gestational week	term	term	term	term	39 weeks	40 weeks	term	term	term	term	term	term	term	term
Neonatal period	low Apgar score at birth	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable	unremarkable
Central Nervous System														
Symptoms that led to specialist evaluation (age)	altered behavior episode: thrashing, did not recognize parents, unable to walk (17 m); acute hemiplegia, letargy, generalized sezures, myoclonic jerks during a febrile gastroenteritis (24 m)	during a viral infection two generalized sezures, choreiform movement disorder (11 m)	myoclonic jerks with flexion of the arms and neck towards the midline with lip smacking (6 m)	myoclonic jerks with uncontrollable thrashing of the limbs (6 m)	during an otitis media, unexplained crying and restlessness with transitory agitation due to walking difficulties (15 m)	slight motor delay, moderate axial hypotonia, instability when sitting, and increased head circumference (8 m)	acute hypotonia (12 m); during infections: acute ataxia, erratic eye movements, agitated behaviour, choreic movements, and transitory ataxia after common flu (3 y)	rapid regression of acquired motor skills and cognition after a 2-day episode of mild diarrhea (12 m)	lethargy and somnolence; a single, brief generalized seizure after a 4-day episode of mild diarrhea (14 m)	acute onset of motor and cognitive regression, choreoathetoid movements whitout prodromal illness prior to the onset of disease	after a minor head trauma, acute onset loss of the milestones and 3 episodes of vacant staring (9 m)	after a minor head trauma, acute onset loss of milestones and generalized tonic seizures	occasional episodes of unsteady gait; ectopia lentis	ataxia and somnolence, lethargy after a febrile illness (18 m)
Global DD / ID after acute onset	DD	DD	DD	DD (normal until 12 m)	no	DD (also before acute onset)	no	borderline level of mental development at Wechsler Mental Development Scale-Revised	severe delay in gross motor development and mild delay in language and social-emotional responses	severe delay in gross and fine motor development, moderate delay in language and social-emotional responses	DD	DD	no	DD
Abnomal muscle tone	hypertonia (spastic hemiparesis)	hypotonia	hypertonia (spastic tetraparesis and opisthotonic posturing)	hypertonia (opisthotonic posturing)	no	hypotonia	no	hypotonia at onset, then mild spasticity of the lower limbs	hypotonia	hypotonia at onset, then hypertonia	hypotonia	hypotonia	no	no
Movement disorder (Hyperkinesia or dystonia)	hyperkinetic movements and dystonia	hyperkinetic movements	no	no	choreo-athetoid movements and hyperkinetic movements	no	hyperkinetic movements during intercurrent illness	no	hyperkinetic movements	hyperkinetic movements	intermittent generalized dystonia and choreic movements	dystonia	no	hyperkinetic movements (tremor)
Nystagmus	NA	no	no	no	no	no	no	no	no	no	no	no	no	no
Ataxia	yes	no	no	no	yes (during intercurrent illness)	no	yes (recurrent during intercurrent illness)	yes	yes	no	no	no	yes (unsteady gait)	no
Seizures	yes	only at the acute onset	yes (epilepsy drug resistant to CBZ-VPA)	yes (epilepsy drug resistant to VPA-nitrazepam)	no	no	no	no	only a single one at the acute onset	no	only at the acute onset	only a single one at the acute onset	no	focal epilepsy
EEG anomalies (at age)	slowed background posteriorly with brief runs of anterior quadrant sharp activity (NA)	normal (12 m)	normal (NA)	normal (NA)	NA	NA	normal (4 y)	NA	NA	NA	NA	NA	NA	focal spike-wave anomalies in the occipital area (left > right) (3 y, 8 y); normal (15 y)
Neuroradiological abnormalities (at age)	NA	CT scan: normal (12 m)	CT scan: temporal lobe and cerebellar atrophy (NA)	CT scan: vermian hypoplasia and enlarged cistern magna (NA)	CT scan: hypodensity of the white matter and frontal lobe (NA)	NA	MRI: bilateral globs pallidus hyperintensity, thin corpus callosum, dilatation of the cerebral arteries (4 y)	MRI: high signal lesions limited to bilateral globus pallidus and substantia nigra (12 m), almost disappeared with age (2 y and 6.5 y)	MRI: high signal lesions limited to bilateral globus pallidus and substantia nigra (14 m), shrunk significantly with age (3 y)	MRI: high signals in bilateral globus pallidus and substantia nigra (16 m), necrotic lesions in the left globus pallidus (16 m), shrunk with age (4 y)	MRI: bilateral symmetrical T2* hyperintense signals in globus pallidus and dentate nuclei of the cerebellum with diffusion restriction (NA)	MRI: hyperintense signals in globus pallidus and dentate nuclei of the cerebellum	MRI: normal (NA)	MRI: hyperintense signals in dentate nuclei of the cerebellum, vermian hypoplasia, slightly dilated fourth ventricle (9 y)
Behavioral anomalies	no	no	no	no	aggressive behaviour	no	two episodes of agitated behaviour during intercurrent illness	no	no	no	no	no	no	behavioral disorder
Organs and Systems														
Visual anomalies	ectopia lentis (4.5 y)	NA	none	ectopia lentis (1.5 y)	none	ectopia lentis	ectopia lentis (3 y 9 m)	none	none	none	none	none	ectopia lentis	none
THERAPY	mild improvement in biochemical and clinical results after low sulfur aminoacid diet	NA	NA	NA	clinical and biochemical improvement under dietary treatment	clinical and biochemical improvement under dietary treatment	low protein diet and thiamine supplementation; however, authors state that the improvement observed may be due to a spontaneous recovery (already observed for previous episodes by the same patient)	dietary therapy was not implemented due to a delayed diagnosis and economic limitations	dietary therapy was not implemented due to a delayed diagnosis and economic limitations	dietary therapy was not implemented due to a delayed diagnosis and economic limitations	antiepileptics, low protein diet, antidystonic medications, and other supportive management	antiepileptics, low protein diet, antidystonic medications, and other supportive management	NA	not yet

Legend: NA, not available; NGS, next generation sequencing; WES, whole exome sequencing; M, male; F, female; m, months; y, years; DD, developmental delay; ID, intellectual disability