month after the initial MRI showed the resolution of the hyperintense signal in bilateral thalamic regions.

WE is a medical emergency raising a risk of irreversible neurological impairment. Prevalence is underestimated. Physicians should be aware of the spectrum of predisposing factors and clinical settings resulting in thiamine deficiency. In patients in whom the disorder is suspected, high-dose intravenous vitamin therapy should be initiated immediately.

Ethics statement

Compliance with ethics guidelines. Informed consent was obtained from the patient for being included in the study. We have received ethics board approval (Comité d'éthique du Groupe Hospitalier du Havre).

Disclosure of interest

The authors declare that they have no competing interest.

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Sensory motor ataxic neuropathy associated dysarthria and ophthalmoplegia "SMANDO" in a consanguineous Moroccan patient with new POLG gene homozygote mutation

A 25-year-old Moroccan man experienced his first symptoms when he was 7 years old with progressive bilateral ptosis. His parents were consanguineous (first degree). His gait had become progressively unsteady with falls and painful paresthesia. His speech was progressively becoming more slurred suggesting a probably associated cerebellar syndrome. Ophthalmologic examination revealed bilateral ptosis (Fig. 1a) with severe ophthalmoparesis in all directions. Gait showed a marked sensory ataxia with a positive Romberg sign. Speech was dysarthric. Motor examination revealed atrophy involving mainly the distal muscles with pes cavus (Fig. 1b and d) and severe proprioceptive impairment. Pectus excavatum (funnel breast) (Fig. 1c) and cleft palate were also present. Electroneuromyography revealed severe axonal predominantly sensory peripheral neuropathy. Skeletal muscle biopsy revealed ragged red fibers (Fig. 1e). Magnetic resonance imaging (MRI) of the brain was normal. The laboratory investigations revealed elevation in serum lactate 886 mg/l (normal: 57–220) and pyruvate 21.66 mg/L (normal: 3.60–5.90). Molecular genetic analysis revealed multiple mitochondrial DNA deletions in muscle tissue detected by the long-range PCR technique. Sequencing of the POLG1 gene revealed the c. 1789C > T (p.Arg597Trp) mutation in the homozygous state. The c. 1789C > T mutation was found in heterozygous form in his consanguineous parents with no manifestation of disease. Based on ACMG guidelines and in silico gene variant tolerance analysis, c.1789C > T (p.Arg597Trp) variant is classified in the ClinVar database as pathogenic/likely pathogenic by three submitters (GeneDx; EGL Genetic Diagnostics [Eurofins Clinical Diagnostics] and Wong Mito Lab [Molecular and Human Genetics, Baylor College of Medicine]). Also, this substitution is located in the linker domain (residues 418–755) which is a highly conserved region. Using four computational methods, a functional impact combined score of 2.65 was obtained by Mutation Assessor classifying the change as "medium". Otherwise, SIFT Polyphen-2 and SNPs&GO software predicted the variant to be deleterious, probably damaging and disease related, respectively.

According to gnomAD, R597 W allele frequency is 0.000006979.

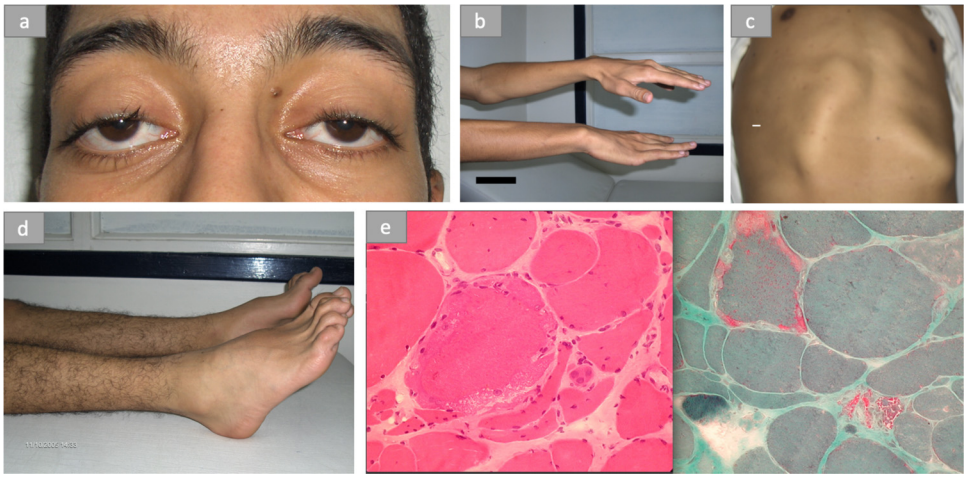

Fig. 1 – Asymmetric ptosis (a). Muscle atrophy (b). Pectus excavatum (funnel breast) (c). Muscle atrophy (d). Muscle biopsy revealed ragged red fibers (e).

The first cases of SANDO were reported in 1997 [1] to describe a novel mitochondrial disease associated with multiple mtDNA mutations in four unrelated patients who presented with sensory ataxic neuropathy, dysarthria and ophthalmoplegia [1]. Since then few cases have been reported. We present the first case of a Moroccan patient with different clinical features of ''SMANDO'' syndrome (Sensory Motor Ataxic Neuropathy ''CMT like'' Phenotype associated dysarthria and Ophthalmoplegia) due to a new POLG gene homozygote mutation that illustrates the phenotypic variability and difficult diagnosis of this syndrome. The pathophysiology of SANDO most often results from mutations in the POLG1 gene [2]. POLG1 usually encodes for DNA polymerase-γ which is important in mitochondrial DNA (mtDNA) replication. There are now over 150 POLG1 mutations known and collectively these mutations result in errors in mtDNA [2,3]. These errors accumulate and cause dysfunction in the respiratory chain of the oxidative-phosphorylation pathway leading to clinical symptoms and findings. SANDO can be either an autosomal recessive or de novo mutation, rarely reported as autosomal dominant. There is a wide phenotypical variation making diagnosis difficult, as was the case in our patient who had a typical manifestation of SANDO, with an important atrophy involving mainly the distal muscles.

There is considerable variability in the phenotype of mitochondrial disease making the diagnosis between different syndromes difficult [4,5]. Mutations in the POLG gene have emerged and they are responsible for a heterogeneous group of multiple syndromes (Alpers syndrome, Ataxia Neuropathy Spectrum disorders, Myoclonus Epilepsy Myopathy Sensory Ataxia, autosomal recessive Progressive External Ophthalmoplegia and autosomal dominant Progressive External Ophthalmoplegia) [6]. There has been no clear correlation between genotype and phenotype in patients with POLG mutations. The p.A467 T mutation in the linker region is the most common mutation. The homozygous p.A467 T mutation shows the emerging spectrum of mitochondrial DNA (mtDNA) stability disorders and enlarging spectrum of sensory ataxic neuropathies associated with mtDNA instability and POLG mutations showing the complex relationship between genotype and phenotype [4,5]. Homozygous mutations of p.W748S and p.E1143G in cis have been reported in patients with ataxia neuropathy without muscle involvement [6].

Disclosure of interest

The authors declare that they have no competing interest.

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Acute dysautonomia and erythromelalgia associated with testicular seminoma: A case report

A 30-year-old man presented with acute-onset hand-and-foot dysesthesia and accommodative dysfunction. He had a non-disseminated testicular seminoma, treated by orchidectomy six months earlier. PET-scan follow-up disclosed a lymph node metastasis two weeks before symptom onset. He had no other medical history, nor did his family, specially no cases of neoplasia or neuropathy. The initial evaluation highlighted manifestations of peripheral dysautonomia: accommodative insufficiency, bilateral mydriasis (Fig. 1 Adie pupil; positive pilocarpine test at 1% and 0.1% dilutions), gastroparesis causing 10 kg weight loss, sympathicotonic orthostatic hypotension, erectile dysfunction and dysuria. He felt continuous local heat with electric discharges and burning sensations elicited by heat sources (showers) and walking. Deep tendon reflexes disappeared in two weeks. Cerebrospinal magnetic resonance imaging, lumbar puncture (including oligoclonal bands and onconeuronal antibodies), ENMG (including sudomotor reflexes) and immunological screening (including anti-Ma2, anti-FGFR3 and anti-a3AChR, but not anti-Kelch-11 antibodies) were negative. The patient underwent exclusive radiotherapy during one month. Meanwhile and during the following two months, the neuropathic pain in the feet worsened despite early treatment with corticosteroids and polyvalent intravenous immunoglobulins. Tramadol, gabapentin, amitriptyline, capsaicin patches, morphine and ketamine could hardly control it. Only cold-water baths, soon permanent, provided relief. A red swelling of the feet was noted before the patient got used to cold-water baths and before he subsequently developed skin ulcerations (Fig. 1 trench foot). ENMG follow-up revealed length-dependent sensorimotor axonal neuropathy: 26.1 to 10.6 μV sensory ulnar nerve amplitude; 67.9 to 11.6 μV sensory sural nerve amplitude. The loss of sudomotor reflexes showed small-fiber impairment. Severe lymphopenia, reaching 100 cells/mm^3, persisted after the intravenous corticosteroids. All clinical features progressively improved three months after onset with no persistent hypermetabolic mass on PET-scan. At ten months, bilateral mydriasis persisted as well as mild paresthesia in the feet and extension deficit of the right toes. All deep tendon reflexes reappeared and ENMG amplitudes were stable. After intensive rehabilitation, the patient achieved complete functional autonomy.

This case illustrates an acute and severe symptomatology associating small- and large-fiber neuropathy and dysautonomia. The monophasic course matching the oncological history is highly evocative of a paraneoplastic syndrome. We found no known onconeuronal antibody. Testicular seminoma is rarely associated with paraneoplastic manifestations: limbic encephalitis, cerebellar ataxia, vertigo. Reported onconeuronal antibodies are anti-Yo, anti-Ma-2, anti-mGluR1 and anti-Kelch-11. To our knowledge, there is only one reported case of neuropathy associated with testicular seminoma [1]. Our case does not match the description of known paraneoplastic autonomic neuropathies like autoimmune autonomic ganglionopathy [2], in which case a3AChR antibodies are found in 30% of patients [3]. Dysautonomia could have impaired vasoreactivity, yielding the hand-and-foot manifestations, evocative of a vascular acrosyndrome: erythromelalgia. Erythromelalgia spectrum associates paroxysmal extreme acral burning pain and swelling triggered by heat and relieved by cold, small-fiber neuropathy and, in 80% of cases, dysautonomia [4,5]. This matches the symptomatology of our case, except the non-paroxysmal symptomatology. In summary, this case evokes an extreme dysregulation of vasoreactivity resulting from an autonomic neuropathy.