mainly occurs in patients with history of thyroid disease, such as goitre and subclinical hypothyroidism, and is infrequent in patients with no underlying thyroid disease, as in our case.[3]

OT is an infrequent neurological disease and its manifestation as a symptom of thyrotoxicosis is extremely rare.[4] The first case was described in 2008; since then, only 3 authors have reported OT or slow OT associated with thyrotoxicosis; onset was not acute or related to contrast administration in any of these cases.[5–7] IIT is described as a high-frequency tremor (14-16 Hz) affecting the trunk and lower limbs, although on occasion it may also affect the upper limbs; it is triggered by standing and causes a feeling described by patients as instability.[4,8]

Ours is the first report of acute-onset OT as the sole symptom of IIT triggered by a cerebral angiography in a patient with no history of thyroid disease. If undetected or untreated, IIT may have potentially fatal consequences. Its incidence may also increase in parallel with the frequency of techniques involving the administration of iodinated contrasts, including brain CT scans, multimodal CT scans, cerebral angiography, and other techniques used in neurological practice. Since it is not possible to accurately identify which patients will develop IIT, and given the lack of preventive measures with proven efficacy, neurologists must be aware of the risk factors and recognise infrequent forms of presentation to ensure effective patient management.[9]

References

1. Hintze G, Blombach O, Fink H, Burkhardt U, Köbberling J. Risk of iodine-induced thyrotoxicosis after coronary angiography: an investigation in 788 unselected subjects. Eur J Endocrinol. 1999;140:264—7.
2. Iakovou I, Zapandiotis A, Mpalaris V, Goulis DG. Radio-contrast agent-induced hyperthyroidism: case report and review of the literature. Arch Endocrinol Metab. 2016;60:287—9.
3. Leung AM, Braverman LE. Iodine-induced thyroid dysfunction. Curr Opin Endocrinol Diabetes Obes. 2012;19:414—9.
4. Labiano-Fontcuberta A, Benito-Leon J, Dominguez-Gonzalez C. Orthostatic tremor: an enigmatic condition. Rev Neurol. 2012;54:425—34.
5. Tan EK, Lo YL, Chan LL. Graves disease and isolated orthostatic tremor. Neurology. 2008;70:1497—8.
6. Lin FC, Wu MN, Chen CH, Huang P. Slow orthostatic tremor as the first manifestation of Grave's disease. Mov Disord. 2013;28:1158—9.
7. Mazzucchi S, Frosini D, Calabrese R, Bonuccelli U, Ceravolo R. Symptomatic orthostatic tremor associated with Graves' disease. Neurol Sci. 2014;35:929—31.
8. Ure RJ, Dhanju S, Lang AE, Fasano A. Unusual tremor syndromes: know in order to recognise. J Neurol Neurosurg Psychiatry. 2016;87:1191—203.
9. Dunne P, Kaimal N, MacDonald J, Syed AA. Iodinated contrast-induced thyrotoxicosis. CMAJ. 2013;185:144—7.

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Epigenetics, memory, and inheritance☆

Epigenética, memoria y herencia

Dear Editor:

In a recent article, Rosales-Reynoso et al.[1] describe the known epigenetic mechanisms involved in memory formation and their role in the aetiopathogenesis of some hereditary neurological diseases. The authors suggest that multiple environmental stimuli lead to epigenetic modifications in the CNS that are critical to short- and long-term behavioural adaptation. According to the study, epigenetic modifications are involved in creating and maintaining behavioural memory on multiple levels. The article explains that CGG trinucleotide repeat expansion and increased DNA methylation in the promoter of the *FMR1* gene prevent gene transcription and the production of messenger RNA and the FMR1 protein in such hereditary neurological diseases as fragile X syndrome.

In one of the first articles on the topic, published in 2010, we analysed the evidence that the number of epigenetic marks (DNA methylations) increases over an individual's life and that such methylations may be sufficiently stable to pass between generations.[2] More recent studies have supported this hypothesis, which has an enormous impact on our understanding of the aetiology of multifactorial diseases, hereditary diseases, and even processes which develop over an individual's entire lifetime, such as memory formation.[3] The methylations occurring in brain neurons, which explain memory formation, are not hereditary since brain tissue is not involved in human reproduction. However, in line with our 2010 article,[2] we suggest that DNA methylations in reproductive cells formed in gonadal tissue, which are potentially inheritable and transmitted from generation to generation, may be involved in CGG trinucleotide repeat expansions and the absence of FMR1 protein expression. The accumulation of methylations in reproductive cells during

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an individual's lifetime may therefore have an impact on the genotype and phenotype of hereditary diseases in their offspring.

These epigenetic marks may be responsible for trinucleotide repeat expansions in various hereditary diseases; treating these disorders constitutes another challenge for medicine today.[4] Much progress is being made in these lines of research in the hope that advancing our knowledge of epigenetics may lead to improvements in the treatment of genetic diseases and those involving environmental factors, as is the case with multifactorial diseases.[5]

References

1. Rosales-Reynoso MA, Ochoa-Hernández AB, Juárez-Vázquez CI, Barros-Núñez P. Mecanismos epigenéticos en el desarrollo de la memoria y su implicación en algunas enfermedades neurológicas. Neurologia. 2016;31:628—38.
2. Landires I. The postdarwinist concept of species. A place for Lamarck. Lancet. 2010;375:806.
3. Morris MJ, Monteggia LM. Role of DNA methylation and the DNA methyltransferases in learning and memory. Dialogues Clin Neurosci. 2014;16:359—71.
4. Qureshi IA, Mehler MF. Understanding neurological disease mechanisms in the era of epigenetics. JAMA Neurol. 2013;70:703—10.
5. Feinberg AP, Fallin MD. Epigenetics at the crossroads of genes and the environment. JAMA. 2015;314:1129—30.

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Congenital myasthenia and congenital disorders of glycosylation caused by mutations in the *DPAGT1* gene☆

Miastenia congénita y defecto congénito de la glucosilación por mutaciones en el gen DPAGT1

Dear Editor:

Protein glycosylation is essential to the correct functioning of numerous biological processes, such as protein folding and stability, intracellular receptor binding, and intracellular communication, among others.[1] Mutations affecting the encoding of certain proteins involved in glycosylation cause defects known as congenital disorders of glycosylation (CDG), which are classified into different subtypes, depending on which point of the process is altered. Most CDGs affect multiple organs and systems. Patients with DPAGT1-CDG (MIM 608093) most frequently present psychomotor retardation, neuromuscular disease, hormonal abnormalities, and dysmorphic features.[2]

Congenital myasthenic syndromes (CMS) are caused by mutations in genes coding for proteins that are essential in maintaining neuromuscular transmission.[3–5] These patients present muscle weakness exacerbated by fatigue; age of onset, distribution of muscle weakness, and treatment response are variable.[3–5] Mutations in the *ALG2*, *ALG14*, *GFPT1*, *GMPPB*,[5] and *DPAGT1* (MIM 614750) genes may cause CMS with predominantly proximal weakness and little facial or eye involvement.[6] *DPAGT1* mutations have traditionally been considered a CDG,[7–9] progressing with slow growth, severe hypotonia, microcephaly, refractory epileptic seizures, and intellectual disability. Wurde et al.[9] report the cases of 2 patients who died within their first year of life. Severe hypotonia in these patients reveals that neuromuscular function was altered. However, another patient group presents symptoms of congenital myasthenia without the other symptoms of DPAGT1-CDG.[9]

We present the case of a 10-year-old patient with 2 *DPAGT1* mutations (compound heterozygote) who presents encephalopathy with symptoms of autism spectrum disorder and CMS (with proximal muscle involvement, no eye or bulbar symptoms), who has responded satisfactorily to treatment with pyridostigmine.

At the age of 10 months, the patient was referred to our department due to symptoms of dysmorphic syndrome, psychomotor retardation, and hypotonia. He had no family history of interest. Our patient's mother had experienced no complications during pregnancy or delivery, and the patient's neonatal period had been normal: weight at birth was 4150 g and Apgar score was 9/10. The newborn blood spot test yielded normal results. The physical examination revealed some dysmorphic features: relative microcephaly, wide forehead, narrow palpebral fissures, widely spaced nipples, and abnormal distribution of fat, predominantly in the trunk and proximal muscles of limbs; limbs were thin in distal regions. He presented significant hypotonia and weakness. Deep tendon reflexes were weak. Psychomotor development was retarded, with the patient achieving head control at 7-8 months and unaided sitting at 2-3 years; however, he was unable to walk unaided. Symptoms have remained stable with no exacerbations over the patient's progression. At the age of 10, he presents severe intellectual

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