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Orthostatic tremor as the only manifestation of thyrotoxicosis following cerebral angiography☆

Temblor ortostático como manifestación aislada de tirotoxicosis tras arteriografía cerebral

Dear Editor:

The use of iodinated contrasts in diagnostic and therapeutic techniques has become increasingly frequent over the past 20 years. These techniques consist in the administration of iodine doses between 90 and several hundred times greater than the recommended daily intake. Iodine-induced thyrotoxicosis (IIT) presents a prevalence rate of 0.05% to 5%, mainly affecting patients with history of thyroid disease; most cases are caused by CT scans with contrast or cardiac catheterisation.[1,2] While such symptoms as cardiac arrhythmia, hyperthermia, tremor, or diarrhoea are frequent in thyrotoxicosis, orthostatic tremor (OT) is exceptional.

We describe an atypical case of acute-onset OT associated with hyperthyroidism secondary to a brain angiography study in a patient with no history of thyroid disease.

Our patient was an 81-year-old male former smoker with a history of hypertension, chronic obstructive pulmonary disease, and atherosclerotic ischaemic stroke of the middle cerebral artery secondary to stenosis of the ipsilateral internal carotid artery. He was being treated with acetylsalicylic acid, clopidogrel, omeprazole, atorvastatin, and amlodipine/hydrochlorothiazide/olmesartan. He was admitted to undergo a cerebral angiography, angioplasty, and stenting of the left internal carotid artery; no immediate complications were observed. Between 48 and 72 hours after the procedure, the patient reported a feeling of instability and presented tremor in all 4 limbs, triggered in the lower limbs by standing. The neurological examination revealed symmetrical postural tremor in the upper limbs, palpable tremor of the lower limbs during standing, and no other abnormalities; these findings are compatible with OT. Results from a systemic examination were normal and palpation of the thyroid revealed no nodules. No alterations were detected in heart rate or temperature, and the patient did not present diarrhoea or any other new symptoms. An analysis of thyroid hormone levels at symptom onset revealed primary hypothyroidism (TSH: 0.04 mU/L; free T4: 2.1 ng/dL; negative antithyroid antibodies). In the absence of other symptoms, the patient continued under clinical follow-up without treatment. A week later, he showed a progressive clinical improvement, with symptoms resolving spontaneously 10 days after onset. A follow-up laboratory test revealed normalised thyroid hormone levels (TSH: 0.30 mU/L; free T4: 1.61 ng/dL).

A typical contrast dose contains approximately 13 500 μg of iodide, which may be released as free iodine in the body. Under normal circumstances, iodine overload causes the Wolff-Chaikoff effect, a self-regulatory mechanism that inhibits iodine organification and thyroid hormone synthesis. Subsequently, at 7 to 10 days, an escape phenomenon occurs and hormone synthesis resumes. Sometimes, iodine overload saturates the self-regulatory mechanism and causes the Jod-Basedow effect, resulting in uncontrolled production of thyroid hormones and IIT. Iodine-induced thyrotoxicosis

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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]

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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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