studies in patients with complex neurodevelopmental disorders of unknown origin.

Funding

The authors have received no funding for this study.

References

1. Li Z, Du C, Zhang C, Zhang M, Ying Y, Liang Y, et al. Novel truncating variant of PPM1D penultimate exon in a Chinese patient with Jansen-de Vries syndrome. Mol Genet Genomic Med. 2020;8:e1120.
2. Jansen S, Geuer S, Pfundt R, Brough R, Ghongane P, Herkert JC, et al. De novo truncating mutations in the last and penultimate exons of PPM1D cause an intellectual disability syndrome. Am J Hum Genet. 2017;100:650—8.
3. Kuroda Y, Murakami H, Yokoi T, Kumaki T, Enomoto Y, Tsurusaki Y, et al. Two unrelated girls with intellectual disability associated with a truncating mutation in the PPM1D penultimate exon. Brain Dev. 2019;41:538—41.
4. Porrmann J, Rump A, Hackmann K, Di Donato N, Kahlert AK, Wagner J, et al. Novel truncating PPM1D mutation in a patient with intellectual disability. Eur J Med Genet. 2019;62:70—2.
5. Adams J, McClellan J, Douglass D, McCurry C, Storck M. Sexually inappropriate behaviors in seriously mentally ill children and adolescents. Child Abuse Negl. 1995;19:555—68.

D. Martín Fernández-Mayoralas[a,c,*], A.L. Fernández-Perrone[a,*], A. Jiménez De Domingo[a], A. Alba Menéndez[b], A. Fernández-Jaén[a,c]

[a] *Departamento de Neuropediatría, Hospital Universitario Quirónsalud, Madrid, Spain*
[b] *Genómica y Medicina, Instituto de Estudios Celulares y Moleculares, Lugo, Spain*
[c] *Facultad de Medicina, Universidad Europea de Madrid, Villaviciosa de Odón, Madrid, Spain*

* Corresponding author.
E-mail addresses: daniel.martinf@quironsalud.es (D. Martín Fernández-Mayoralas), afernandezj@quironsalud.es (A.L. Fernández-Perrone).

https://doi.org/10.1016/j.nrleng.2020.06.005
2173-5808/

Sweating as a presentation of focal epilepsy: clinical case report*

Sudoración como presentación de epilepsia focal: descripción de un caso clínico

Dear Editor:

Autonomic symptoms may be the first manifestation of an epileptic seizure.[1] The International League Against Epilepsy (ILAE) classification identifies autonomic seizures as focal non-motor seizures.[2] Autonomic symptoms may range from subclinical changes to potentially fatal haemodynamic instability. The anatomical substrate of autonomic seizures generally resides in the central autonomic network. This network comprises the insular cortex, anterior cingulate cortex, amygdalae, hypothalamus, periaqueductal grey matter, parabrachial nucleus, solitary nucleus, rostral ventrolateral medulla, and raphe nucleus.[3] We present the case of a patient with episodes of right hemibody hyperhidrosis secondary to insular dysplasia.

The patient was a 39-year-old right-handed man with no relevant medical history. From the age of 28, he had presented episodes of increased temperature and sweating on the right side of the face and body; episodes lasted 5-10 minutes and did not involve altered level of consciousness (Fig. 1 and Appendix B). These episodes presented 6-7 times per day. The baseline sleep-deprived electroencephalogram (EEG) showed no epileptiform alterations. A brain magnetic resonance imaging (MRI) study (3T scanner) revealed radiological signs suggestive of polymicrogyria of the left insular cortex (Fig. 2). Suspecting focal autonomic seizures, we started treatment with eslicarbazepine acetate at 800 mg/day; this reduced the number of seizures to the

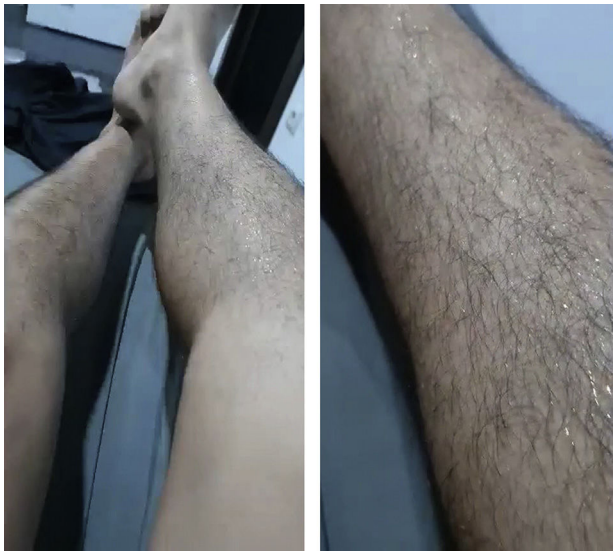

Figure 1 Sweating in the patient's right lower limb during an epileptic seizure.

* Please cite this article as: López-Bravo A, Sanabria-Sanchinel AA, Marín-Gracia M, Viloria-Alebesque A. Sudoración como presentación de epilepsia focal: descripción de un caso clínico. Neurología. 2021;36:332—334.

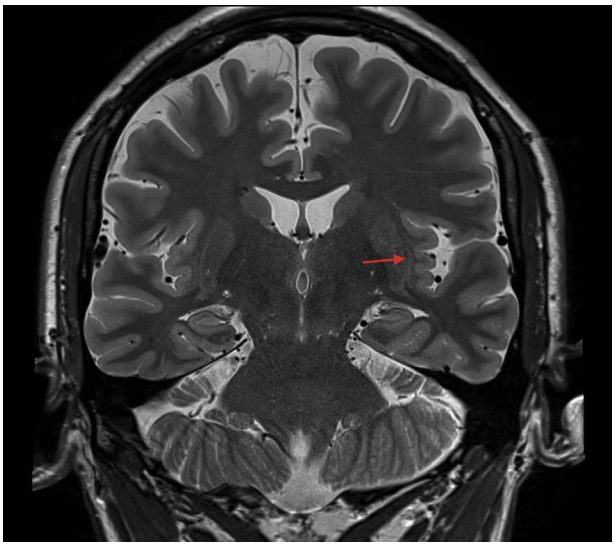

Figure 2 T2-weighted brain MRI sequence (coronal plane) showing prominence of the left Sylvian fissure and polymicrogyria of the left insular cortex.

current frequency of one episode per month. Dosage is currently being adjusted; no video EEG monitoring has been performed due to a lack of availability at our centre and the good response to treatment.

Autonomic symptoms frequently present during seizures, either as the predominant manifestation or in association with other convulsive symptoms. They may be classified as cardiovascular changes, and respiratory, gastrointestinal, skin, pupillary, genitourinary, or sexual manifestations.[4] Some of these signs and symptoms may help us to locate and lateralise the area of seizure onset and the subsequent route of propagation. They may also assist in understanding the anatomical and functional organisation of the central autonomic network.[4]

Previously described cutaneous manifestations include flushing, pallor, sweating, and piloerection. Autonomic symptoms have been attributed to different aetiologies: Franco et al.[5] reported a patient with ipsilateral facial sweating secondary to anti-Ma2 autoimmune encephalitis associated with testicular teratoma. Sweating in the context of seizures has also been reported in a patient with a basal forebrain malformation, in association with tremor and hypothermia.[6] Cases have also been reported of generalised sweating with other vegetative symptoms, with one case secondary to a periventricular lesion extending to the limbic area,[7] and another as a consequence of a parietal meningioma.[8]

Previous cases have also been reported of episodes of hyperhidrosis and ictal piloerection of autoimmune origin in the temporal lobe. Other structures participating in the central autonomic network have less frequently been associated with pilomotor seizures.[9] We present the first case of seizures presenting with hyperhidrosis and no piloerection, contralateral to insular polymicrogyria. Insular epilepsy is difficult to diagnose due to its clinical heterogeneity: with the exception of nociceptive symptoms, no clinical presentation is very specific of this location; autonomic symptoms have been described in this clinical entity.[10] On many occasions, conventional EEG does not reveal alterations due to the deep location of the insula, which makes it necessary to perform video EEG monitoring in the event of treatment resistance.[10] In our patient, the purely autonomic clinical presentation led us to consider the insula as a possible site of seizure onset, given its role in the central autonomic network; while non-specific, the absence of pathological data on the EEG may be compatible with alterations in this location, and the detection of a structural alteration in the MRI study together with the good response to antiepileptic drugs make us consider this diagnosis probable. One limitation of this study is the lack of video EEG monitoring or stereo EEG, which may help establish a more accurate electro-clinical correlate.

In conclusion, we present a case of autonomic seizures with hyperhidrosis probably caused by contralateral insular polymicrogyria. We consider it important to systematically describe more patients with infrequent autonomic symptoms, such as sweating, in order to establish the potential of these symptoms to locate and lateralise lesions.

Funding

The authors have received no external funding for this study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.nrleng.2020.06.009.

References

1. Freeman R, Schachter SC. Autonomic epilepsy. Semin Neurol. 1995;15:158—66.
2. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the International League Against Epilepsy: position paper of the ILAE Commission for classification and terminology. Epilepsia. 2017;58:522—30.
3. Cersosimo MG, Benarroch EE. Central control of autonomic function and involvement in neurodegenerative disorders. Handb Clin Neurol. 2013;117:45—57.
4. Baumgartner C, Koren J, Britto-Arias M, Schmidt S, Pirker S. Epidemiology and pathophysiology of autonomic seizures: a systematic review. Clin Auton Res. 2019;29:137—50.
5. Franco AC, Noachtar S, Rémi J. Ictal ipsilateral sweating in focal epilepsy. Seizure. 2017;50:4—5.
6. Klein CJ, Silber MH, Halliwill JR, Schreiner SA, Suarez GA, Low PA, et al. Basal forebrain malformation with hyperhidrosis and hypothermia: variant of Shapiro's syndrome. Neurology. 2001;56:254—6.
7. Cortés V, Landete L, Gómez E, Blasco R. [Partial simple vegetative crisis: importance of electroencephalographic findings]. Rev Neurol. 1997;25:1931—3.
8. Mendler MH, Sautereau D, Pillegand B, Ravon R. A case of digestive epilepsy with late diagnosis: a disease not to be disregarded. Gastroenterol Clin Biol. 1998;22:235—9.

9. Rocamora R, Becerra JL, Fossas P, Gomez M, Vivanco-Hidalgo RM, Mauri JA, et al. Pilomotor seizures: an autonomic semiology of limbic encephalitis? Seizure. 2014; 23:670—3.
10. Jobst BC, Gonzalez-Martinez J, Isnard J, Kahane P, Lacuey N, Lahtoo SD, et al. The insula and its epilepsies. Epilepsy Curr. 2019; 19:11—21.

A. López-Bravo[a,b,*], A.A. Sanabria-Sanchinel[c], M. Marín-Gracia[b,c], A. Viloria-Alebesque[b,d]

[a] *Departamento de Neurología, Hospital Reina Sofía, Tudela, Navarra, Spain*
[b] *Instituto de Investigación Sanitaria de Aragón (IIS-A), Zaragoza, Spain*
[c] *Departamento de Neurología, Hospital Clínico Lozano Blesa, Zaragoza, Spain*
[d] *Departamento de Neurología, Hospital General de Defensa, Zaragoza, Spain*

* Corresponding author.
E-mail address: alba.lopez.bravo@gmail.com
(A. López-Bravo).

https://doi.org/10.1016/j.nrleng.2020.06.009
2173-5808/

Progressive cerebellar ataxia with falsely positive anti-Ma2 antibodies*,**

Ataxia cerebelosa progresiva con anticuerpos anti-Ma2 falsamente positivos

Dear Editor:

Aetiological diagnosis of adult-onset ataxia represents a diagnostic challenge, and ruling out potentially treatable causes must be a priority.[1] Among these, we may highlight paraneoplastic neurological syndromes (PNS), given the significance of their association with an underlying tumour. However, misdiagnosis may lead to iatrogenic complications secondary to unnecessary immunosuppression. We present the case of a patient with late-onset progressive ataxia, which was initially diagnosed as a PNS but finally found to be of degenerative origin.

The patient was a 65-year-old man with no relevant family or personal history with the exception of smoking and dyslipidaemia, who consulted in 2017 due to a 2-year history of progressive gait disorder. The examination revealed scanning speech, fragmented saccades, bilateral appendicular dysmetria, mild truncal ataxia, and moderate gait ataxia. He reported no alcohol abuse or exposure to other toxic substances. A brain MRI scan revealed pontine and cerebellar atrophy with no other relevant findings (Fig. 1). Laboratory analysis returned positive results for anti-Ma2 antibodies in the serum (Immunoblot, EUROIMMUN AG) and slightly increased tumour markers (carcinoma embryonic antigen, 10.2 ng/mL [normal range, 0-3.4]; squamous cell carcinoma antigen, 2.0ng/mL [0-1.5]); the remaining parameters, including autoimmunity, vitamins (B_1, B_{12}, and E), and cerebrospinal fluid analysis (including antineuronal antibody determination), yielded normal results. The patient was diagnosed with cerebellar ataxia of paraneoplastic aetiology, although test results for occult malignancy (cervical/thoracic/abdominal/pelvic CT scan, genitourinary ultrasound, colonoscopy, bronchoscopy, and PET) were negative throughout the 2 following years. We initially treated the patient with intravenous immunoglobulins (IVIg), and subsequently with a megadose of corticosteroids; as no benefit was observed, we started treatment with rituximab in June 2018. Despite this, his symptoms continued to worsen over the course of 2018: he needed walking aids and developed dysphagia, cognitive impairment, tremor, urinary incontinence, and REM sleep behaviour disorder. In early 2019, the patient showed signs of parkinsonism and autonomic dysfunction worsened (orthostatic hypotension and vasomotor changes in the hands). We decided to discontinue immune therapy and to reconsider his diagnosis; we requested a new determination of anti-Ma2 antibodies at our centre (Immunoblot, EUROIMMUN AG), once more returning weakly positive results, and simultaneously at a reference laboratory (immunohistochemistry on rat cerebellum; IDIBAPS, Hospital Clínic, Barcelona), which yielded negative results. Furthermore, we requested a brain SPECT study, which revealed bilateral dopaminergic hypometabolism (Fig. 2). All these data suggested a final diagnosis of cerebellar-type multiple system atrophy. The patient started symptomatic treatment with levodopa and physical therapy, with a poor response. Unfortunately, the patient died in May 2019. The family did not agree to an autopsy study.

Cerebellar degeneration is one of the most frequent PNS (up to 40% of cases),[2] and usually presents a subacute course with rapid clinical deterioration over less than 12 weeks. Neuroimaging results may be normal or reveal mild cerebellar atrophy, and cerebrospinal fluid analysis usually indicates inflammation (pleocytosis, high protein level, or IgG oligoclonal bands). It has been reported in association with different tumours and onconeuronal antibodies targeting intracellular antigens, with anti-Ma antibodies rarely

* Please cite this article as: Fernández Díaz E, Sánchez-Larsen Á, Redondo-Peñas I, Segura T. Ataxia cerebelosa progresiva con anticuerpos anti-Ma2 falsamente positivos. Neurología. 2021;36:334—336.

** The early progression of this case was communicated in poster format at the 69th Annual Meeting of the Spanish Society of Neurology, held in Valencia from 21 to 25 November 2017, under the title ''Chronic paraneoplastic cerebellar degeneration with positive anti-Ma2 antibodies.''