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F. Ruiz-Botero[a,*], E. Gómez-Pineda[a], H. Pachajoa[a,b]

[a] *Centro de Investigación en Anomalías Congénitas y Enfermedades Raras, Facultad de Ciencias de la Salud, Universidad Icesi, Cali, Colombia*
[b] *Fundación Clínica Valle del Lili, Cali, Colombia*

* Corresponding author.
E-mail addresses: feliperuizb@hotmail.com, fruiz@icesi.edu.co (F. Ruiz-Botero).

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Ischaemic stroke as the predecessor event of an episode of thrombotic thrombocytopenic purpura☆,☆☆

Ictus isquémico como evento predecesor de brote de púrpura trombótica trombocitopénica

Dear Editor,

Thrombotic thrombocytopaenic purpura (TTP) is an infrequent haematological disease characterised by thrombocytopaenia and haemolytic anaemia. Neurological complications are relatively frequent during the development of the disease, and manifest after onset of clinical and analytical haematological symptoms.[1] We present the case of a woman with TTP whose neurological complications (recurrent ischaemic strokes) preceded a new episode of TTP activity.

Our patient is a 36-year-old woman diagnosed with TTP in 1998 after presenting multiple haematomas in the context of microangiopathic haemolytic anaemia and thrombocytopaenia. Due to acute-onset dysarthria and weakness in the right limbs, she was admitted to the neurology department with suspected acute ischaemic stroke. The neuroimaging study revealed focal hypoperfusion in the left parietal region, with no filling of the distal M2 segment of the left middle cerebral artery. A follow-up MRI scan revealed multiple acute punctiform ischaemic lesions in the left temporo-parietal region (Fig. 1). The aetiological study revealed no blood alterations (Table 1) or paroxysmal disorders of heart rate (normal Holter ECG and telemetry findings), and a transoesophageal echocardiography ruled out the presence of cardioembolic sources. We diagnosed ischaemic stroke of undetermined cause and recommended antiplatelet treatment (acetylsalicylic acid) at discharge. Fifteen days after the first admission, the patient presented dysaesthesia in the face and right hand. In this instance, neuroimaging studies (CT and MRI) did not reveal acute alterations. The laboratory analysis only revealed the presence of isolated schistocytes (low schistocyte levels might be considered normal in healthy individuals, not suggesting disease), with no other pathological findings (Table 1). Seven days after the second event, she presented symptoms of asthenia with haematomas in the lower limbs. A new analysis revealed thrombocytopaenia and haemolytic anaemia. Matrix metalloproteinase ADAMTS13 activity was 0% (normal activity, 6%-100%), and the anti-ADAMTS13 IgG antibody titre was 80 IU/mL (Table 1). After diagnosis of a TTP episode, treatment was started with plasma exchange, corticosteroids, and rituximab, with the patient showing a progressive improvement in both clinical and analytical parameters.

TTP is a rare haematological disease whose neurological manifestations occur during the development of the disease (including stroke and transient ischaemic attacks).[1] We present a patient whose cerebral ischaemic events preceded the haematological changes typical of active TTP, which is extremely infrequent.[2—6] Thrombotic complications of TTP are caused by an immune-mediated phenomenon which causes the inactivation of the ADAMTS13 metalloprotease enzyme, responsible for degrading high-molecular-weight Von Willenbrand factor multimers. Accumulation of those

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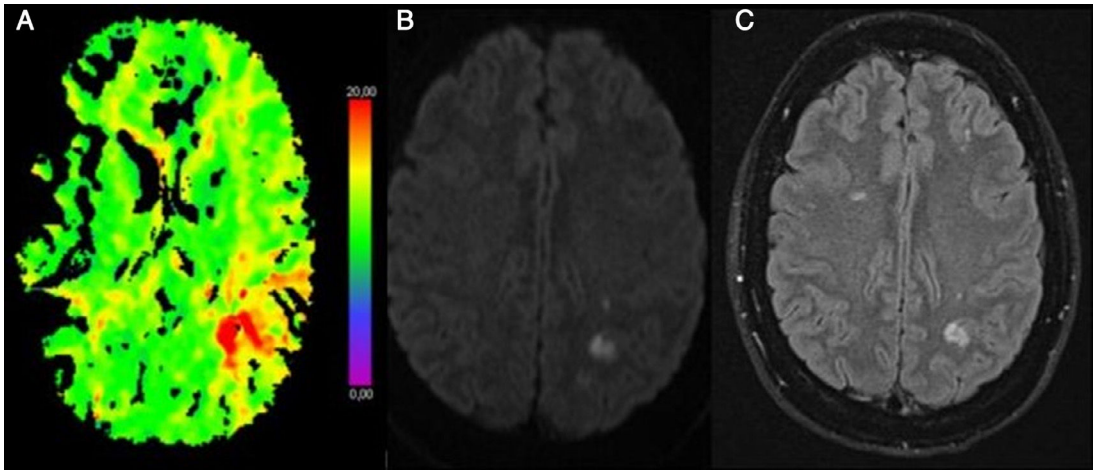

Figure 1 (A) CT perfusion sequence. Time to peak: delay in the posterior territory of the left middle cerebral artery. (B) MRI diffusion-weighted sequence. Cortical and subcortical diffusion restriction in the left parietal region. (C) MRI FLAIR sequence. Left parietal cortico-subcortical lesion (shown in the diffusion-weighted sequences) and bilateral frontal lesions with longer progression times.

Table 1 Laboratory findings obtained during the different hospital admissions and after immunosuppressive treatment.

	Normal range	First admission	Second admission	Third admission	After immunosuppressive treatment
Haematocrit (%)	36-51	37	36	18	31
MCV (fL)	80-100	90.1	88.9	83.3	95.7
Platelets ($\times 10^9$/L)	130-400	213	164	17	618
Indirect bilirubin (mg/dL)	<0.6	0.4	0.4	1.2	0.2
LDH (U/L)	250-450	412	374	888	441
Blood smear	Normal	Normal	Very isolated schistocytes	12-15 schistocytes per high-power field	5—6 schistocytes per high-power field
ADAMTS13 activity (%)	6-100	Not determined	Not determined	0	0
Anti-ADAMTS13 IgG antibodies (IU/mL)	Negative	Not determined	Not determined	Positive (80)	Negative

LDH: lactate dehydrogenase; MCV: mean corpuscular volume.

multimers predisposes to platelet aggregation, causing thrombosis at the microvascular level.[7,8] Likewise, we cannot rule out that the cerebral ischaemic event triggered the TTP episode, since the literature includes reports of ischaemic stroke-induced coagulation alterations resembling the changes reported in patients with no history of TTP (decreased ADAMTS13 activity in the acute phase).[9] Regarding the antithrombotic management of these complications, it should be noted that clopidogrel may act as hapten for anti-ADAMTS13 IgG antibodies in patients with a baseline autoimmune mechanism; therefore, there must be clear justification for its use for preventing new ischaemic events in patients with a history of TTP.[10]

In conclusion, we should consider TTP as an infrequent cause of stroke in young or middle-aged women, even in the absence of the haematological and analytical changes typical of the disease. In the follow-up of patients already diagnosed with TTP, the appearance of focal neurological signs without abnormal laboratory results at the time of diagnosis should prompt physicians to begin periodic monitoring of platelet and erythrocyte levels. Finally, determining ADAMTS13 activity and anti-ADAMTS13 antibody titres may be useful for early diagnosis.

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M. Vicente-Pascual[a], C. Zamora-Martinez[b], S. Amaro-Delgado[a,*]

[a] *Servicio de Neurología, Hospital Clínic de Barcelona, Barcelona, Spain*
[b] *Servicio de Medicina Interna, Hospital Clínic de Barcelona, Barcelona, Spain*

* Corresponding author.
E-mail address: samaro@clinic.cat (S. Amaro-Delgado).

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Spanish cultural adaptation of the short version of the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ-23)☆

Adaptación cultural al español del cuestionario sobre las dificultades para trabajar con esclerosis múltiple. Versión corta de 23 ítems (MSWDQ-23)

Dear Editor,

Numerous studies have addressed the impact of multiple sclerosis (MS) on patients' work.[1] Most of these approach the question from a solely economic perspective, however: they calculate the number of days per year patients are absent from work due to MS and the indirect costs associated with work-related problems, and analyse the relationship between the level of disability (EDSS) and total cost due to MS.[1,2] In contrast, few studies address the specific professional difficulties facing MS patients and how these problems are perceived.[3] Furthermore, these studies use non-validated instruments, tools not specifically designed to evaluate work-related problems, or instruments that evaluate a limited set of difficulties.[1,3]

The Multiple Sclerosis Work Difficulties Questionnaire is a self-administered instrument evaluating the impact of MS on patients' professional lives; both the original 50-item version and the more recently developed shorter version (MSWDQ-23) have good psychometric properties.[4,5] Both were initially developed in English by a group of neuropsychologists from the University of New South Wales (Australia). The MSWDQ-23 contains 23 items with 5 response options (from 0 [never] to 10 [almost always]), which assess how frequently patients experienced difficulties in their current or most recent jobs over the previous 4 weeks. Items are grouped into 3 dimensions: physical, psychological/cognitive, and external barriers. The total scores for each dimension and for the questionnaire as a whole range from 0 to 100, with higher scores indicating greater difficulty. Patients' perception of cognitive barriers in the workplace, as measured with the MSWDQ-23, has been reported to be predictive of unemployment and reduced work hours since MS diagnosis.[6]

We describe the process of cultural adaptation of the MSWDQ-23 to the Spanish-speaking population. The adaptation followed the recommendations made by the International Society for Pharmacoeconomics and Outcomes Research[7]: (1) preparation, (2) forward translation, (3) reconciliation, (4) back translation, (5) back translation review, (6) harmonisation, (7) cognitive debriefing, (8) review of cognitive debriefing results, and (9) proofreading (Fig. 1).

Two independent native Spanish-speaking translators independently translated the questionnaire; the project coordinator subsequently reconciled the 2 translations with the assistance of the translators. The Spanish-language version introduced some language changes in the instructions

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