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LETTER TO THE EDITOR

Atypical presentations of thrombotic thrombocytopenic purpura in middle-aged women with recurrent cerebral macrovascular thrombosis: a case report

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Dear Editor,

In the current clinical practice, minimal criteria to define thrombotic thrombocytopenic purpura (TTP) are the presence of signs of microangiopathic haemolytic anaemia and low platelet (PLT) count [1]. TTP relapses (20–50 % of cases) are defined as the recurrence of acute TTP symptoms 30 days after the first episode, while exacerbations occur within 30 days [2]. We here report on an atypical case of acquired TTP where minimal criteria were met only after many recurrent macrovascular ischemic events.

A 42-year old Caucasian woman with a history of coronary and cerebral ischemic events was admitted on June 2013, following a recurrent transient ischemic attack (TIA). She had severe anaemia and thrombocytopenia with laboratory signs of intravascular haemolysis and mild renal impairment. In her past medical history, recurrent ischemic events occurred from 2008 to 2012, without known risk factors and regardless of treatment. The patient was treated with acetyl salicylic acid (100 mg daily) after the first ischemic event (stroke, in 2008) plus anticoagulation with warfarin after the third stroke (in 2010), with a good compliance . Screening for autoimmune disease, Factor V Leiden and Factor II (G20210A) gene mutations and circulating anticoagulants were normal. Blood cell count and peripheral blood smear did not show any significant abnormalities in the past, without evidence of schistocytes; a slight decrease in PLT count (92×109/L) was observed only once (in 2012), at that time, ADAMTS13 activity (ADAMTS-13: AC) was 65 %. At the current admission, ADAMTS-13: AC was 6 %, inhibitors were at high titer (2 Bethesda Units, BU). A genetic test for Upshaw-Schülman syndrome was normal. Therapeutic plasma exchange (TPE) and prednisone (1 mg/kg body weight) treatment was started and maintained until clinical and haematological remission [3]. TPE (Gambro®, Italy) was performed daily for 3 weeks with an increase of ADAMTS13: AC to 50 %. TTP exacerbated after 10 days, it was well controlled with weekly rituximab (375 mg/m^2 body surface), for 4 weeks. A relapse occurred after 37 days with the patient presenting seizures: ADAMTS-13: AC, which was 54 % after the last treatment, had decreased to 6 %. A second course of weekly rituximab, followed by maintenance with azathioprine (50 mg twice daily for 10 days, then 50 mg, daily) was followed by clinical and haematological remission. Rituximab was re-administered for its previous rapid efficacy and to prevent further complications [4]. The patient is alive and free from recurrences for 18 months; azathioprine maintenance is still on course. ADAMTS-13: AC is monitored every 4 months, and it ranges from 45 to 51 %; inhibitors are no longer detectable.

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Table 1 Clinical features at presentation of atypical TTP in young and middle aged women

Publication	Age	Relapse	Clinical features	Hb g/dL	Plt x 1000/mmc	ADAMTS-13	Schistocytes	Creatinine mg/dL	Treatment
Lucchesi et al.	42	2	Stroke (seizure)	7.5 (10.9–11.7)	24 (107–120)	6 %	present	1.3 (1.1)	PEX, CS (PEX, RTX, AZA)
Imanirad et al.[5]	40	1	MI, stroke	11.7 (14.4)	34 (49)	<5 %	rare	1.4 (1.2)	PEX, CS (PEX, CS, RTX)
Imanirad et al.[5]	25	1	Stroke (vague neurol. sympt.)	9.4 (12)	27 (40)	<5 %	rare	1.2 (1.1)	PEX (PEX, RTX)
Imanirad et al.[5]	68	9	Seizure (stroke, seizure)	7.4 (9.3–14.4)	27 (61–130)	NA (<5 %)	rare/present	0.9 (0.6)	PEX, CS (PEX, CS, splenectomy, RTX)
Imanirad et al.[5]	58	1	Seizure (stroke)	8 (14)	14 (180)	NA (<5 %, 6 %)	present/rare	1.3 (1)	PEX, CS, RTX
Idowu et al.[6]	48	2	Stroke (stroke)	8 (13.2)	20 (113)	16 %	no	NA (0.8)	PEX (PEX)
Downes [8]	42	Multiple	Stroke (stroke)	10 (NA)	207 (NA)	12 %	no	NA	PEX
Downes [8]	40	4	Stroke (MAHA)	9.3	239	NA	rare	NA	PEX
Tsai [9]	36	Multiple	Stroke (stroke)	Normal	Normal	<0.1[a]	no	NA	PEX+CS+RTX
O'Brien [10]	28	1	TIA (ecchymoses)	Normal	71	NA	present	0.7	PEX
O Brien [10]	44	2	TIA (stroke)	12.4	205	NA	NA	1.0	PEX+CS

Clinical feature and treatment columns: *Brackets* report information related to symptoms and treatment at relapse, *PEX* plasma exchange, *CS* corticosteroid, *RTX* rituximab, *AZA* azathioprine, *MAHA* microangiopathic haemolytic anaemia, *MI* myocardial infarction, *NA* not available, *Neurol* neurological, *TIA* transient ischemic attack

[a] Tsai reports ADAMTS13 activity =<0.1 U/mL

We hypothesize that the disease occurred in 2008, with a chronic relapsing behaviour and a more acute phase only in 2013. Ten similar cases have been reported [5–10] (Table 1). In atypical TTP recurrences, symptoms mainly guide treatment at recurrence. Most of the described cases recovered after the administration of rituximab or immunosuppressive agents.

Our case was especially atypical because it became manifested only after years during which even minimal criteria for TTP diagnosis were not met and ADAMTS13: AC was normal.

When macrovascular ischemic events are not accompanied by anaemia or thrombocytopenia, TTP is rarely taken into account.

However, TTP should be considered even with only slight laboratory and haematological abnormalities.

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Conflict of interest The authors declare that they have no conflict of interest.

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