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A Case Report of Thrombotic Thrombocytopenic Purpura Associated with Systemic Lupus Erythematosus: Overlapping Features

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Abstract The association between thrombotic thrombocytopenic purpura (TTP) and systemic lupus erythematosus (SLE) is rare. Herein, we present a case with overlapping features between TTP and SLE. A 17-year old girl admitted to our hospital with an initial complaint of high grade fever, persistent headache, and microangiopathic hemolytic anaemia (negative Coombs test with schistocytes), thrombocytopenia with thrombotic event with central nervous system involvement and probably renal involvement. Also, our patient fulfilled the criteria for SLE- fever, hair loss, oral ulcers, central nervous system involvement, renal involvement, positive ANA, positive dsDNA and normal C3 and C4. The patient was rescued by extensive plasma exchange started promptly after the diagnosis. After 8 months of treatment, TTP recurred, successfully managed with plasma exchange, steroids and cyclophosphamide. It was difficult to discriminate TTP from SLE. Our case presented simultaneous features of both SLE and TTP who reinforce the importance of early diagnosis of TTP by the observation of fragmented RBCs and the intensive therapy, including plasma exchange and careful follow-up, not only to ensure diagnosis and treatment of a relapsed episode of TTP, but also to ensure proper management of the patient's physical and mental health due to its high morbidity.

Keywords: *thrombotic thrombocytopenic purpura (TTP), systemic lupus erythematosus (SLE) and plasma exchange*

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1. Background

Thrombotic thrombocytopenic purpura (TTP) is a challenging disorder for hematologists because survival is only 10% without plasma treatment and it is associated with a high risk of major complications. The incidence of TTP appears to have increased, presumably due to heightened awareness of the syndrome [1,2,3,4].

TTP is a rare hematologic syndrome first described in 1924 by Eli Moschowitz who used the term acute pleiochromic anemia with hyaline thrombosis of terminal arterioles and capillaries [5]. In 1966, a pentad of severe thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, renal insufficiency, and fever was established [6]. These symptoms may, also be present in SLE relapses. Although TTP and systemic SLE are distinct entities, they may appear as overlapping clinical syndromes [7].

TTP has been rarely reported in SLE patients also its manifestation may occur before lupus diagnosis [8], at presentation [9], or during the course of the disease [10]. So it is important to distinguish between the two diseases because of the therapeutic implications.

Recently, a mechanism for platelet consumption in TTP has been elucidated. A deficiency of ADAMTS-13 or an autoantibody directed against it is responsible for some cases of TTP, leading to platelet aggregation and thrombosis [6]. Nevertheless? it is neither sufficiently sensitive nor specific to determine the decision to initiate or withhold PEX [11].

Our case presented simultaneous features of both SLE and TTP who reinforce the importance of early diagnosis, early aggressive treatment and careful follow-up for patients with TTP not only to ensure diagnosis and treatment of a relapsed episode of TTP, but also to ensure better outcomes in the patient's physical and mental health due to its high morbidity.

2. Case Report

A previously healthy 17-year-old girl was admitted to Sohag University Hospital in December 2013 because of a history of generalized fatigue, oral and nasal spontaneous

bleeding, bruising over the upper and lower extremities as well as headaches with moderate grade fever and rapidly progressive thrombocytopenia, but no signs of bleeding from others orifices. The review of systems was only positive for recent increased hair loss, but otherwise negative. Her menstrual periods were regular and predictable and she did not have any significant past medical or surgical history.

On physical examination: Her body temperature was of 38.2°C, pulse was fast and regular at 100 beats/min, blood pressure of 130/80 mmHg, respiration at 16 per minute and body weight was 58 kg. She was fully alert and oriented, but with icterus, pale skin and with bruising on upper and lower extremities. Cardiovascular examination revealed only tachycardia but no added sounds, and her abdomen was soft without tenderness or hepatosplenomegaly on palpation. The rest of the physical examination was unremarkable.

At that moment, Laboratory findings revealed thrombocytopenia with hemolytic anemia. The serum hemoglobin level was low at 6.3 g/dL (normal range; 12.0–16.0 g/dL), hematocrit 20.1%, MCV 89.0 fL, reticulocytes 14% after correction 6.6%, her platelet count was also low at 54.8 K/uL (normal range; 150–450 K /uL), white blood cell (WBC) count 11,400/mm³. Peripheral blood smear test clearly revealed few schistocytes, anisocytosis, poikilocytosis, and some tear drop cells. The serum level of lactate dehydrogenase(LDH) was elevated to 4831 U/L (normal; 141– 247 U/L), and that of total bilirubin level was also elevated at 4.9mg/dL (normal range; 0.2–1.1mg/dL) with dominant elevation of indirect bilirubin 3.1mg/dL, serum albumin level was 3.7g/dl, aspartate aminotransferase (AST) 127 U/L (normal 0–41) U/L, alanine aminotransferase (ALT) 20 U/L (normal 0–41), the erythrocyte sedimentation rate was 1st hour 69 - 2nd hour 112 and uric acid 15.5mg/dl (normal 3.4-7), thus suggesting hemolytic anemia. Both the direct and indirect Coombs tests were negative. The patient's bone marrow cells obtained by aspiration revealed normal differentiation.

Although the serum levels of fibrinogen degradation products (FDP) and D-dimers were elevated to > 9000 ng/mL (normal range; less than 500 ng/mL), suggesting DIC, the other parameters related to DIC, such as the serum level of fibrinogen, prothrombin time (PT), and activated partial thromboplastin time (aPTT) were normal. The blood urea nitrogen (BUN) and creatinine levels (0.9 mg/dl) were within the normal range in the first day but in second day, the patient had fever and disturbed consciousness. Her Glasgow Coma Scale (GCS) was 13 - Drowsy without focal neurological deficit. She hadn't had any seizures and creatinine level was elevated (1.2 mg/dl) associated with oliguria. Urinalysis showed albumin (+3), granular casts and RBCs 16-20/HPF. She had normal C-reactive protein, CSF and brain computer tomography. Her Rheumatoid Factor and antistreptolysin-O Test were negative. Serum electrolytes and arterial blood gases were normal. Serologies for HBV & HCV and HIV were negative.

A summary of the laboratory tests on admission is shown in Table 1.

She was admitted to the Intensive Care Unit, and treatment was started with methylprednisolone 1 gram intravenously daily for 3 days. Despite medical treatment, the patient had progressive disturbed consciousness GCS: 12, anaemia (haemoglobin level, 5.2 g/dL) and thrombocytopenia (platelet count 43.8 K/uL), serum creatinine concentration increased to (1.57 mg/dl), then, (1.9 mg/dl) L, and the serum lactate dehydrogenase concentration increased to 4983 U/L. ECHO and Abdominal U/S was normal except swollen kidneys.

Table 1. Laboratory test results on admission

Blood test				
WBC	11,400 /mm³	D-Coombs		Negative
Neutrophils	58%	Indirect Coombs		Negative
Lymphocytes	25%	HBsAg		Negative
Monocytes	2%	HIV		Negative
Metamyelocytes	8%	Anti HCV		Negative
Band cells	3%	RF		Negative
RBCs	1.62 M/uL	CRP		Negative
Retic	6.6%	C3		110 (Normal)
Hb	6.3 g/dL	C4		15 (Normal)
Hct	20.1%,	ANA		Positive
MCV	89.0 fL	Anti-DNA		Positive
PLT	54.8 K/uL	ANCA(cyt)		Negative
D-D	> 9000 ng/mL	ANCA(nuc)		Negative
ESR 1st h	69	PT		11.8
ESR 2nd h	112	PPT		32 sec
TP	7.2 g/dL	ASOT		Negative
AlB	3.7g/dl	lupus anticoagulant		0.77 Negative
Cr	0.9 mg/dL	anti-SS-A antibodies		Negative
UA	15.5mg/dl	anti-RNP antibodies		Negative
Na	138mmol/L	anticardiolipin	IgM	Negative
			IgG	Negative
K	4.3mmol/L	CSF		Normal
CL	102mmol/L	Proteins electrophoresis		Normal
T-Bil	4.9 mg/dL	HDL		28 mg/dl
D- Bil	1.1 mg/dL	Cholesterol		144 mg/dl
AST	127 U/L	Triglycerides		376 mg/dl
ALT	20 U/L	GLU (fasting)		121
LDH	4831 U/L	Bone marrow		Normal

On admission, thrombotic microangiopathy (TMA), SLE, seronegative autoimmune hemolytic anemia with thrombocytopenia (EVANS syndrome), CAPS, and DIC were considered as possible candidates for her thrombocytopenia with hemolytic anemia. We provisionally diagnosed her illness as TMA with complicated autoimmune disorder because of a negative Coombs test, hemolytic anemia with schistocytes and thrombocytopenia, and intravenous methylprednisolone (1 gram, 3 days) administration followed by oral administration of prednisolone (60mg/day), were initially introduced but treatment did not ameliorate her illness, therefore, we suspected TTP. Plasma exchange therapy was immediately added to her treatment. Her symptoms and the abnormal findings of laboratory tests slightly improved (platelet count 93 K/uL) and the creatinine level fell to 1.1 mg/dl after first session. However, she had persistent neurological sequelae with seizures and uncontrolled

hyperglycemia (serum glucose 457 mg/dl) and another brain computer tomography was done which was normal. Plasma exchange therapy was continued in the second day and her symptoms gradually disappeared.

As expected, additional laboratory tests showed that her antinuclear antibody (ANA) test and anti-DNA antibodies were positive.

She did not have positive results to lupus anticoagulant, ANCA (cytoplasmic and perinuclear), anti-SS-A antibodies, anti-RNP antibodies, and anticardiolipin antibodies.

Also, her serum complement levels were normal (C3; 110 mg/dL, and C4; 15 mg/dL, normal range; C3 85–160 mg/dL, C4 12–38mg/dL).

Serum proteins electrophoresis was normal and serum Cholesterol was 144 mg/dl, HDL: 28 mg/dl, Triglycerides: 376 mg/dl and Alb/creatinine ratio 32 micro g Alb/mg creatinine. Patient could not afford anti-platelet antibody, hence was not done.

One week after plasma exchange initiation, she developed ulceration over the hard palate.

The patient's condition improved gradually after 10 days. Plasmapheresis was gradually discontinued after 8 session without TTP relapsing.

She improved remarkably, with a normalization of her platelet count in 15 days, and her liver enzymes, LDH, and hemoglobin all were corrected within 4 weeks. She was discharged without any symptoms.

After two months of treatment, renal biopsy was done which showed mesangial proliferation (lupus nephritis class II with no residual of TMA).

Thus this patient had microangiopathic hemolytic anaemia with thrombocytopenia with thrombotic event with fever, central nervous system involvement and probably renal involvement. Also patient fulfilled the criteria for SLE-fever, hair loss, oral ulcers, central nervous system involvement, renal involvement, positive ANA and positive dsDNA and negative anti-phopholipid antibody. Hence a diagnosis of SLE with TTP was made.

Table 2. A summary of clinical course of the patient

Day after admission	1	2	3	5	7	10	28
HB (g/dL)	6.2	5.2	6.8	7.9	8.2	9.6	11.2
Platelets	54.8	43	93	170	140	303	232
LDH	4831	4983	2651	1234	682	548	462
Creatinine	0.9	1.2	1.57	1.9	1.1	0.9	0.6

Prednisone dose was progressively tapered to 15 mg/day. She was followed up for 8 months, and her hematocrit, platelet count and LDH remained normal with TTP remission.

Nine months after first episode, reduced vision in left eye was developed and one week later the patient was admitted to Sohag University Hospital again because of history of generalized fatigue, headaches with moderate grade fever and rapidly progressive thrombocytopenia, after complete investigations a relapsed episode of TTP was diagnosed with inflammation of left eye vitreous body, and she was given a combination treatment including plasma exchange for 8 days, methylprednisolone 1000 mg/d for 3 days, then 80 mg/d and cyclophosphomide. Her condition improved rapidly with a normalization of her platelet count in 19 days.

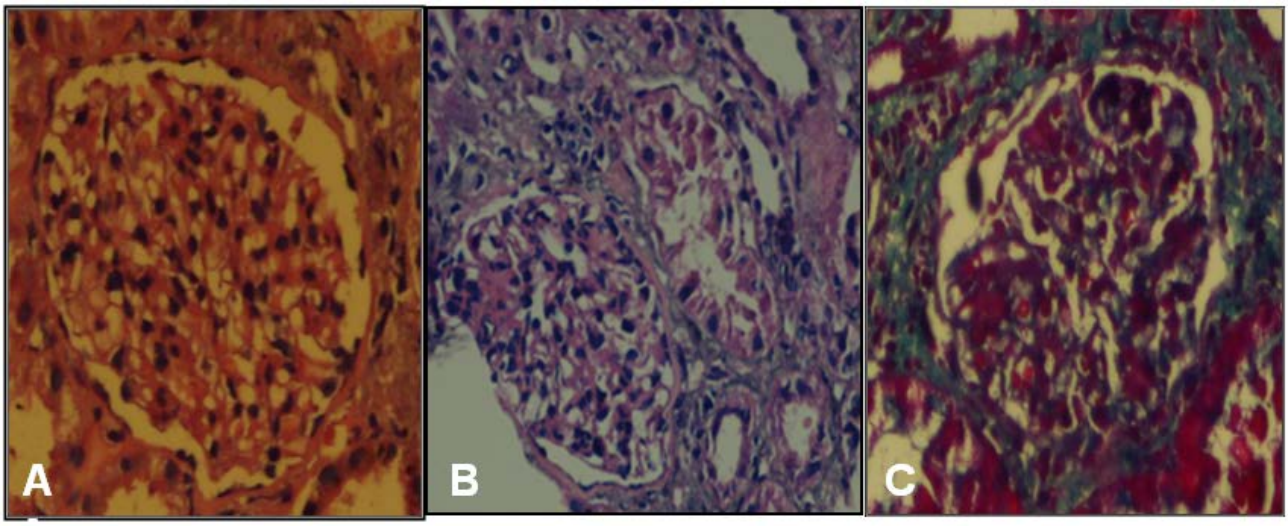

Figure 1. Histopathology of lupus nephritis class II. High power view (A,B) H&E and (C) Masson stain: A light micrograph of a glomerulus shows mild mesangial cell proliferation in SLE patient with history of Thrombotic microangiopathy

3. Discussion

TTP is a rare and severe manifestation in patients with SLE, although the relationship between these two conditions has not been well defined. Our case showed two major problems caused by the association of SLE and TTP. The first is the difficulty in diagnosis, because the clinical presentation may be mistaken for signs of SLE itself: hemolytic anemia, thrombocytopenia and abdominal pain. SLE and TTP share similar clinical symptoms. The fragmentation of red blood cells is essential to categorize microangiopathic hemolytic anemia. The absence of a positive Coombs' test, along with the other symptoms, thrombocytopenia and neurological involvement support the diagnosis of TTP and require urgent plasma exchanges [12], whereas its effectiveness in SLE is controversial [13]. Therefore, the differential diagnosis is very important, although their similarities in clinical manifestations sometimes make it very difficult. However, effective

treatments for them are different. Plasma exchange is now considered the most effective for TTP

The clinical overlap between these two syndromes has been described more commonly in young women, as the case described [14]. The possible differential diagnosis and the clinical differences among representative TMA including TTP are hemolytic-uremic syndrome(HUS), catastrophic anti-phopholipid antibody syndrome, EVANS syndrome and disseminating intravascular coagulopathy.

Our patient had not shown any digestive symptoms; but HUS is characterized as renal diseases and usually associated with bacterial colitis (Escherichia coli O157 and Shigella-toxin-producing strain). HUS can be distinguished from TTP by diarrhea (D+HUS). However, diarrhea negative (D-HUS) cases of HUS have been reported.

The detection of RBC bound immunoglobulin G and complement by the direct antiglobulin test (DAT; Coombs test) is useful in the diagnosis of AIHA [15].

A small number of patients with AIHA have been reported to show a negative Coombs test [16], probably because of the lower affinity of IgG to RBC [17].

Like our case, autoimmune disorder occasionally makes it difficult to diagnose TTP. More-over, it may be difficult to distinguish TTP from the other types of TMA. Therefore, the lack of these autoantibodies cannot conclusively exclude AIHA and/or EVANS syndrome, but our patient did not improved with pulse steroid treatment.

Coombs test in our patient was negative and EVANS syndrome is characterized by autoimmune hemolytic anemia (AIHA) with autoimmune thrombocytopenia is also considered as one of important differential diagnosis from TTP.

The absence of a positive Coombs' test, along with the other symptoms, thrombocytopenia and neurological involvement, support the diagnosis of TTP and require urgent plasma exchanges as in our patient. An initial schistocyte count of more than 1% in the absence of any other cause of thrombocytopenia is strongly suggestive of TTP. Elevated titers of ANA, the presence of lupus anticoagulant, and a positive Coombs' test reaction are among the American College of Rheumatology classification criteria for SLE and therefore, especially if seen in combination, are suggestive of SLE. Although the ACR classification criteria for SLE are >90% specific and sensitive, the clinical presentation of isolated TTP may be indistinguishable from that of SLE with secondary TTP during the acute initial episode of TTP [18].

Our patient did not have positive results to lupus anticoagulant, ANCA, anti-SS-A antibodies, anti-RNP antibodies, and anticardiolipin antibodies, so that catastrophic antiphospholipid syndrome (CAPS) which is an accelerated from APS [19] is currently difficult.

In fact, laboratory findings in our patient revealed positivity for ANA and dsDNA However, the diagnosis of CAPS was not likely in the present case because of negative of aCL.

Regarding DIC, our patient was thought to have SLE with an elevation in the serum levels of FDP and D-dimer, suggesting DIC. Although the pathogenesis of DIC in SLE patients is still not fully understood, vasculitis has been considered to be involved in the pathogenesis of DIC in patients with SLE [20]. Immune complexes (ICs) activated by complements may injure the vascular endothelial cells, resulting in the release of tissue thromboplastin [20,21]. Therefore, discrimination of TTP from a certain case with SLE may be difficult in such cases as the present case.

In These situations, tests of the ADAMTS-13 activity seem to be the most useful for the diagnosis in TTP. Fujimura and Matsumoto categorized TTP using plasma levels of ADAMTS13 activity (<3%; severe, 3–25%; moderate, 25–50%; mild) for the purpose of distinguishing TTP from TMA. They also reported that the levels of ADAMTS-13 activity are lower in idiopathic TTP than in secondary TTP [22]. Generally, patients with autoimmune diseases tended to a have mild-to-moderate deficiency in ADAMTS-13 activity. In addition, Coppo et al. reported that patients with severe ADAMTS-13 deficiency in adult idiopathic TMA are characterized by various autoimmune manifestations, a lower platelet count, and mild renal involvement [23].

During the last decade, the main pathophysiologic feature of TTP has been described as severe deficiency of von Willebrand Factor (vWF) cleaving metalloproteinase (ADAMTS-13), which normally cleaves the unusually large vWF into smaller and less adhesive vWF moeity. This deficiency is thought to be possibly secondary to the presence of an IgG antibody inhibiting ADAMTS-13 activity, inhibition that finally allows the presence of units of unusually large vWF which is responsible for the microvascular thrombosis, hemolysis, and thrombocytopenia [24].

Connective tissue disorders, including SLE, can present with low levels of ADAMTS-13, suggesting a possible common pathophysiology for these diseases [25].

The diagnosis of TTP is based on the presenting clinical features. Measurements of ADAMTS13 activity are not required and may not be appropriate for the critical initial management decision to begin or not begin plasma exchange.

Severe ADAMTS13 deficiency does not identify all patients who may respond to plasma exchange treatment, some patients with severe ADAMTS13 deficiency may have other disorders, and different assay methods may vary in their detection of patients with severe deficiency [26].

Although our patient was diagnosed as SLE and was treated by steroid, they were not sufficiently effective for her symptoms, so that her main symptoms were thought to have been caused by her TTP, and plasma exchange treatments were performed, and she dramatically improved.

Plasma exchange continues to be the main stay of treatment in patients with TTP, even when concomitant SLE is present. Treatment with plasma exchange has greatly improved the prognosis and mortality has decreased from 85%–100% to 10%–30% [24]. This resulted in the diagnostic criteria to be revised from the earlier pentad to the current dyad of thrombocytopenia and microangiopathic hemolytic anemia, with no clinically apparent alternative explanation for thrombocytopenia and anemia [28,29,30].

However, there are refractory cases and relapses occurs in 40% of patients. In these situations various immunosuppressive agents, including rituximab (RTX), have been employed [31].

Other therapies that have been used with variable results include high-dose steroids, cytotoxic agents such as cyclophosphamide and vincristine, and intravenous immunoglobulin. Rituximab, a monoclonal antibody against CD20 receptor, has been used in four reported cases of refractory TTP in SLE patients, with a response and disease- specific survival of 50% [32,33,34]. Pugnoux et al. have reported that plasma exchange has beneficial effects for SLE-related diseases such as neurolupus, alveolar hemorrhage, and severe lupus nephritis [35]. Furthermore, Cerdas-Quesada has reported that refractory AIHA was successfully treated with plasma exchange [36].

K. Hamasaki et al. report reviewed Summary of reported cases complicated with SLE and TTP [37] and we added a summary of new reported cases upto 2013 (Table 3).

Table 3. Summary of reported cases complicated with SLE and TTP

	Age	Sex	Initial Diagnosis	SLE	Prognosis	CS	PE	Other	Author	Year
1	16	F	SLE	Active	Died	-	-		Alpert 38	1968
2	39	F	SLE	Active	Died	+	-		Dekker 39	1974
3	17	M	SLE	Active	survived	+	+		Dekker39	1974
4	17	F	SLE	Active	survived	+	+		Oen 40	1980
5	35	F	SLE	Inactive	died	+	-		Cecere 41	1981
6	12	F	TTP	-	survived	-	-	AZ	Gatenby 42	1981
7	27	F	SLE	Active	survived	+	+	AZ, CY	Finkelstein 43	1982
8	38	F	SLE	Inactive	survived	+	+		Becker 44	1985
9	31	F	SLE	Inactive	survived	+	-		Dixit 45	1985
10	50	F	SLE	Inactive	survived	+	+		Gelfand 46	1985
11	21	F	SLE	Active	survived	+	+	CY	Gelfand46	1985
12	40	F	SLE	Active	survived	+	+	CY	Fox 47	1986
13	42	F	SLE	Active	Died	+	+		Fox 47	1986
14	47	F	SLE	Inactive	survived	+	-	VCR, IVIG	Itoh 48	1990
15	31	F	SLE	Inactive	Died	+	+	CY	Itoh 48	1990
16	10	F	TTP	Active	survived	-	+		Jonsson 49	1990
17	19	F	SLE	active	survived	-	+	IVIG	Hess 50	1992
18	32	F	SLE	active	survived	-	+	IVIG	Hess 50	1992
19	30	F	TTP	-	survived	-	+		Simeon-Aznar 51	1992
20	41	F	SLE	Inactive	survived	+	+	CY, IVIG	Stricker 52	1992
21	22	F	SLE	active	Died	-	+	CY, VCR, IV	Braun 53	1993
22	20	F	SLE	Unknown	Died	-	-	VCR	Porta 54	1993
23	26	F	SLE	Unknown	survived	-	+	CY	Porta 54	1993
24	52	F	SLE	unknown	Died	-	+	CY	Porta 54	1993
25	26	F	SLE	Unknown	Died	-	+	VCR	Porta 54	1993
26	30	F	TTP	-	survived	-	+	CY, VCR	Bray 55	1994
27	71	F	SLE	active	survived	-	+		Jain 56	1994
28	48	F	SLE	active	survived	-	+		G Jain	1994
29	30	F	SLE	active	Died	-	+	CY, VCR	Jain	1994
30	56	F	SLE	Inactive	survived	+	-		Jain	1994
31	28	M	SLE	Inactive	Died	-	+	VCR	Jain	1994
32	66	F	SLE	Inactive	survived	-	+	CY	Jain	1994
33	38	F	SLE	active	Died	-	+		Nesher 57	1994
34	35	F	SLE	active	survived	-	+		Nesher	1994
35	27	F	Simultaneous	active	survived	-	+		Nesher	1994
36	39	F	Simultaneous	Active	survived	-	+		Nesher	1994
37	23	F	TTP	-	Survived	-	+		DiPietro 58	1996
38	25	M	Simultaneous	active	survived	+	+	CY	Kaloterakis 59	1996
39	24	M	Simultaneous	active	survived	-	+	CY	Lim 60	1996
40	17	M	TTP	-	survived	-	+	CY	Myung61	1996
41	14	F	Simultaneous	active	Died	+	+	CY	Caramaschi 62	1998
42	35	F	Simultaneous	active	survived	+	+	VCR, IVIG	Caramaschi	1998
43	52	F	SLE	active	survived	+	+		Caramaschi	1998
44	41	F	SLE	Inactive	Died	+	+	CY	Jorfen 63	1998
45	32	F	SLE	Inactive	Died	+	+	IVIG	Jorfen	1998
46	46	F	Simultaneous	active	Died	-	+	CY	Musio 43	1998
47	16	F	SLE	inactive	survived	+	+	VCR, IVIG, C	Perez-Sanchez 64	1999
48	17	M	Simultaneous	active	survived	+	+	VCR, CY	Perez-Sanchez	1999
49	38	F	SLE	active	Died	+	+		Musa 65	2000
50	23	F	TTP	-	survived	+	+		Musa	2000
51	33	F	Simultaneous	active	Died	+	+		Nanke 66	2000
52	12	F	Simultaneous	active	survived	+	-		Gungor 67	2001
53	15	F	Simultaneous	active	suvivied	+	+		Sakarcan 68	2001
54	34	F	Simultaneous	active	Died	+	+		Y Vaidya 69	2001
55	39	F	SLE	active	Survived	+	+		Vaidya	2001
56	39	M	SLE	Active	Survived	+	+		K. Hamasaki 37	2003
57	30	F	SLE	active	Survived	+	+	MMF	Pratish 70	2008
58	15	F	SLE	Active	Survived	+	*	CY	Risa Yamada 71	2011
59	20	M	SLE	Active	Survived	+	+	MMF, RTX	Selma 72	2012
60	10.4	F	SLE	Active	Survived	+	+	Chloroquine	Campos 73	2013
61	10.5	M	SLE	active	Survived	+	+	chloroquine	Campos 73	2013

CS; corticosteroid, PE; plasmapheresis or plasma-exchange, AZ; azathiopurine, CY; cyclophosphamide, VCR; vincristine, IVIG; intravenous immunoglobulin G infusion, MMF; Mycophenolate mofetil and RTX; rituximab

K. Hamasaki et al. report reviewed Summary of reported cases complicated with SLE and TTP (case 1-55) [37].

The sequence of events observed in our case triggers the question of how useful it would be to screen patients that present with suspected TTP with ANA. Although SLE may present with hemolytic anemia, thrombocytopenia, neurologic deficits, fever, and renal insufficiency, the finding of fragmented RBCs or schistocytes favors the diagnosis of TTP [74].

The underlying reason for the association of SLE with TTP is unknown. There is still considerable debate about whether certain antiphospholipid antibodies or lupus anticoagulant play a pathogenic role in triggering TTP in SLE patients, although neither of these two types of antibodies has to be present for SLE patients to develop TTP [75].

The relationship between the ADAMTS-13 inhibitor and SLE also needs to be further investigated, since its presence in patients with SLE and concomitant TTP had not been described in the few small retrospective series available because the test was not available at that time

The association of SLE and TTP is uncommon, but potentially lethal, even with current treatment strategies, emphasizing the importance of early diagnosis and aggressive management with plasma exchange and immunosuppression.

The early recognition of TTP in this patient and the prompt workup of her associated underlying disease allowed an early effective treatment and follow up, improving the immediate outcome, but also rituximab (RTX) should be employed to prevent relapse and improve long-term prognosis.

The possible limitation in our case could be lack of some investigation. A future prospective and multicentre study is necessary.

4. Conclusion

We believe that the pathogenesis and association of SLE with TTP still remain poorly understood and the findings of this case report will highlight the importance of early diagnosis and early aggressive treatment for patients with TTP to avoid a poor outcome by decreasing morbidity and mortality.

5. Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying figures.

6. Disclosure

No financial grants or funding sources were used. There is no conflict of interest for any authors of this manuscript.

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