Mod Rheumatol (2004) 14:174–178
DOI 10.1007/s10165-004-0287-4

CASE REPORT

**Haruo Abe · Norioki Tsuboi · Sonosuke Yukawa
Souichirou Tsuji · Haeru Hayashi · Naoichiro Yukawa
Hirofumi Takanashi · Koichiro Tahara
Norihiko Tonozuka · Tohru Hayashi**

Thrombotic thrombocytopenic purpura complicating Sjögren's syndrome with crescentic glomerulonephritis and membranous nephritis

Received: March 26, 2003 / Accepted: December 12, 2003

Abstract The association of either thrombotic thrombocytopenic purpura (TTP) or crescentic glomerulonephritis with Sjögren's syndrome is rare. We report a case of TTP appearing after the diagnosis of Sjögren's syndrome with crescentic glomerulonephritis and membranous nephropathy. Circulating immune complex was detected, and immune complex deposits were shown along the capillary walls of renal biopsy specimens. Despite steroid pulse therapy and plasma exchange therapy, the patient died. The etiology of TTP is unclear. This case is important when considering the etiology of TTP related to autoimmune disease.

Key words Crescentic glomerulonephritis · Immune complex (IC) · Membranous nephropathy (MN) · Sjögren's syndrome (SS) · Thrombotic thrombocytopenic purpura (TTP)

Introduction

Thrombotic thrombocytopenic purpura (TTP), first described by Moschowitz in 1924,[1] is manifested clinically by the pentad of microangiopathic hemolytic anemia, thrombocytopenia, fluctuating neurological abnormalities, renal involvement, and fever. The characteristic pathological findings are diffuse hyaline thrombi composed of fibrin and platelet in arterioles and capillaries; endothelial damage has been proposed as the pathogenetic process.[2] Among the numerous etiological possibilities[3,4] are prostaglandin I_2 stabilization factor deficits, the presence of immune complex (IC), platelet-agglutinating protein, drugs such as cyclosporin A, chemotherapeutic agents, a gene abnormality, infection (endotoxin, human immunodeficiency virus), and von Willebrand factor (vWF) abnormalities due to antibodies that inhibit vWF-cleaving protease[5,6]; however, no absolute cause has yet been proven.

H. Abe (✉) · N. Tsuboi · S. Yukawa · S. Tsuji · H. Hayashi · N. Yukawa · H. Takanashi · K. Tahara · N. Tonozuka · T. Hayashi
Third Department of Internal Medicine, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan
Tel. +81-3-3342-6111; Fax +81-3-5381-6653
e-mail: haruoa@aqua.plala.or.jp

Our report presents a case of TTP complicating acute crescentic, rapidly progressive glomerulonephritis. The patient also had membranous nephropathy (MN) and Sjögren's syndrome (SS). Among the various possibilities, this case may indicate that, at least in some cases, the etiology of TTP is closely related to an immune abnormality.

Case report

A 75-year-old woman suddenly developed macroscopic hematuria. After 12 days, the urine test showed a protein concentration of 1 g/dl and numerous red blood cells (RBCs) in each microscopic field. Laboratory blood examination revealed serum creatinine 1.27 mg/dl, blood urea nitrogen (BUN) 15.3 mg/dl, serum albumin decreased to 2.7 g/dl, and serum cholesterol increased to 271 mg/dl. After another 11 days, her serum creatinine increased to 2.39 mg/dl and the BUN to 32.4 mg/dl. She was then admitted to our hospital.

Laboratory blood examination on admission revealed the following results: serum creatinine 3.49 mg/dl, BUN 125.5 mg/dl, creatinine clearance 10.97 ml/min, glutamic oxaloacetic transaminase (GOT) 29 IU/l, glutamic pyruvic transaminase (GPT) 17 IU/l, lactate dehydrogenase (LDH) 775 IU/l, creatinine phosphokinase (CK) 117 U/l, total protein 5.6 g/dl, albumin 2.4 g/dl, total bilirubin 0.65 mg/dl, direct bilirubin 0.07 mg/dl, indirect bilirubin 0.58 mg/dl, white blood cell (WBC) count 12000/μl, hemoglobin 10.5 g/dl, hematocrit 31.5%, and platelet count 31.5×10^4/μl.

The antinuclear antibody (ANA) titer was >1:1280 (homogeneous and speckled pattern), and the anti-DNA antibody (radioimmunoassay) was 1.5 IU/ml (normal ≤6 IU/ml). The anti-Sm antibody was negative, anti-Ro/SSA antibody was 1:64, and anti-La/SSB antibody was 1:32.

Complement C3 was 31 mg/dl (normal 60–115 mg/dl), and C4 was 10 mg/dl (normal 15–50 mg/dl). CH_{50} was 18.0 U/ml (normal 25–50 U/ml). Circulating IC C1q was <1.5 μg/ml (normal <3.0 μg/ml), and circulating IC anti-C3d antibody was >40 μg/ml (normal ≤13 μg/ml).

The following test results were all negative: direct and indirect Coombs test, cryoglobulin, proteinase-3 anti-neutrophil cytoplasmic autoantibodies (PR3-ANCAs), myeloperoxidase anti-neutrophil cytoplasmic autoantibodies (MPO-ANCAs), anti-cardiolipine β_2-glycoprotein I antibody, lupus anticoagulant, and anti-glomerular basement membrane (GBM) antibody. Urinalysis revealed conspicuous hematuria and 2.86 g/day protein.

Daily treatment with 300 mg dipyridamole and 60 mg prednisolone was initiated on hospital day 3.

She had repeated symptoms of dryness of the eyes and mouth. Salivary gland scintigraphy revealed hypofunction of bilateral submaxillary glands. A minor labial gland biopsy showed periductal infiltration of more than 50 lymphocytes (focus score 2) with acinar atrophy. Based on these observations and the fact that the serum anti-SS-A and anti-SS-B antibody assays were both positive, primary SS was diagnosed. Because renal biopsy showed crescentic glomerulonephritis (CrGN) and early MN (Figs. 1–3), we decided that the present therapy was insufficient and so initiated hemodialysis, methylprednisolone pulse therapy (1 g/day for 3 days), and double-filtration plasmapheresis on hospital day 15. Although these therapies alleviated the hypergamma-globulinemia and edema, the hypocomplementemia and renal deficits did not improve following the daily administration of 300 mg dipyridamole and 60 mg prednisolone.

Subsequently, thrombocytopenia appeared. On hospital day 24, blood examination revealed the following results: platelet count 8.8×10^4/μl, WBC count 15 900/μl, hemoglobin 10.0 g/dl, GOT 38 IU/l, GPT 26 IU/l, LDH 904 IU/l, CK 204 U/l, total protein 4.0 g/dl, albumin 2.6 g/dl, total bilirubin 0.95 mg/dl, direct bilirubin 0.28 mg/dl, indirect bilirubin 0.67 mg/dl, haptoglobin 217 mg/dl (normal 41–273 mg/dl).

The bone marrow smear showed no abnormalities; therefore, methylprednisolone pulse therapy (500 mg/day for 3 days) was added on hospital day 26. Oral steroids were also given (40 mg of prednisolone daily except on the days of pulsed intravenous methylprednisolone). Although the platelet count and hemoglobin level gradually increased, the hypocomplementemia and renal deficits did not improve. On hospital day 53, the laboratory reported the following: C3 28 mg/dl, C4 16 mg/dl, CH_{50} 22.1 U/ml, platelet count 15.8×10^4/μl, WBC count 15 000/μl, and hemoglobin 13.4 g/dl.

The prednisolone was tapered, with the dosage being decreased to 30 mg/day on hospital day 57. However, her body temperature increased to 38.0°C, and her level of consciousness changed from apathetic to soporific. The laboratory investigations on hospital day 62 showed the following: platelet count 4.3×10^4/μl, WBC count 14 100/μl, hemoglobin 11.0 g/dl, LDH 1888 IU/l, GOT 44 IU/l, GPT 24 IU/l, CK 121 U/l, total bilirubin 2.47 mg/dl, direct bilirubin 0.87 mg/dl, indirect bilirubin 1.67 mg/dl, and haptoglobin <10 mg/dl; the peripheral blood smear showed many burr and helmet cells (Fig. 4).

Disseminated intravascular coagulation was ruled out owing to the increased fibrinogen level and the absence of a prolonged prothrombin time. The clinical features were most consistent with TTP. Her platelet count was 2.4×10^4/μl, and her LDH increased to 2090 IU/l on hospital day 65. Plasma exchange (PE), sodium ozagrel, and prostacyclin were initiated in addition to the hemodialysis. Unusually large vWF multimers were not detected in her plasma.

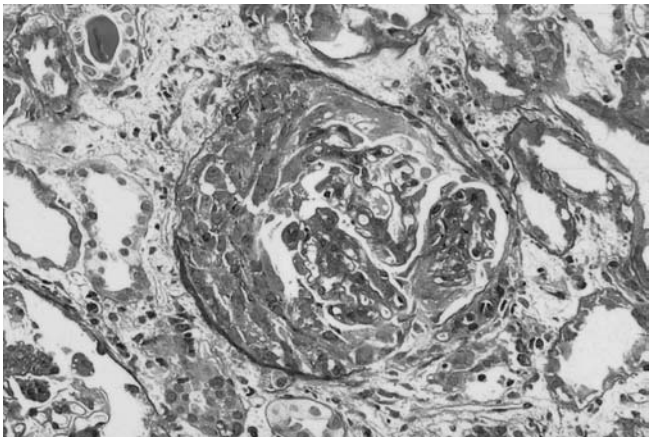

Fig. 1. Renal biopsy specimen. Light microscopy showed that 70% of all glomeruli had cellular crescentic changes. PAS ×200

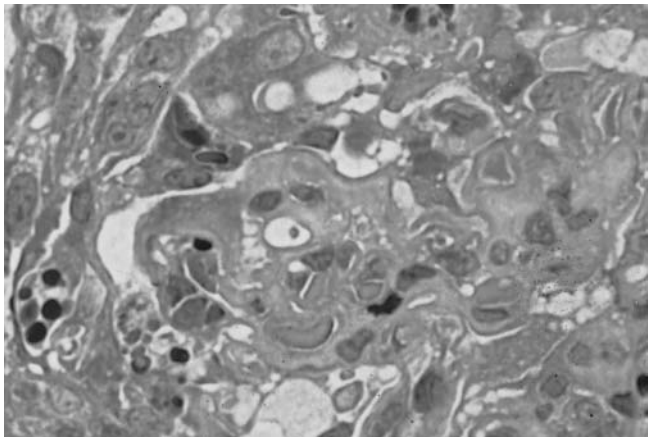

Fig. 2. Renal biopsy specimen. Immune deposits are evident in the mesangial matrix and subepithelium. Masson's trichrome stain ×600

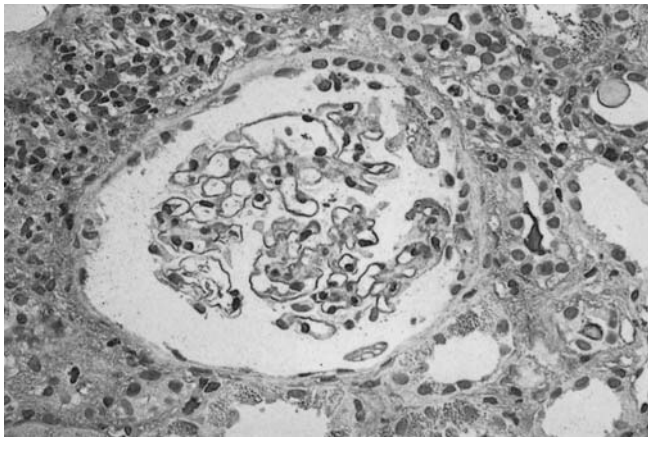

Fig. 3. Renal biopsy specimen. Immunoglobulin G chiefly showed a peripheral pattern similar to that of complement C3. PAP stain ×200

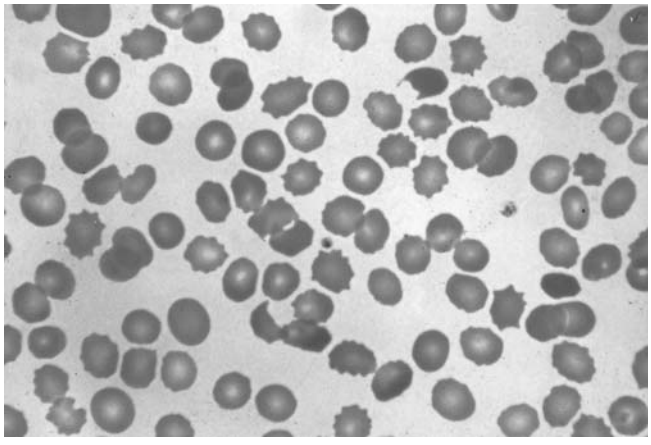

Fig. 4. Peripheral blood smear shows many burr and helmet cells

After PE (on hospital days 65, 67, 68), her state of consciousness improved, her LDH values decreased to 1230 IU/l, and the thrombocytopenia and hypocomplementemia improved slightly: platelet count $3.3 \times 10^4/\mu l$, C3 42 mg/dl, C4 12 mg/dl, CH_{50} 23.3 U/ml on hospital day 68.

Tonic convulsions unresponsive to anticonvulsant drug therapy developed on day 70, her state of consciousness deteriorated, and the blood pressure fell. Her platelet count became $7.9 \times 10^4/\mu l$, WBC count 10 300/μl, hemoglobin 10.5 g/dl, LDH 1852 IU/l, GOT 81 IU/l, GPT 2 IU/l, CK 252 U/l, C3 21 mg/dl, C4 8 mg/dl, and CH_{50} 24.4 U/ml. Brain computed tomography (CT) showed no significant abnormal findings, and her state of consciousness and blood pressure quickly improved. A similar attack occurred again, however, with haphazard changes in blood pressure. Plasma infusion was initiated on hospital day 71. The next day her platelet count was $7.2 \times 10^4/\mu l$, hemoglobin 8.8 g/dl, and LDH 1719 IU/l. She died from sudden cardiac arrest on hospital day 72. Autopsy was not permitted.

Discussion

Most case reports of TTP complicating collagen vascular disease (CVD) have been of patients with systemic lupus erythematosus (SLE).[7] TTP with SS is rare. Individual cases of TTP preceding the diagnosis of SS,[8] SLE,[9] or systemic sclerosis[10] have been reported. These reports contain the suggestion that in some cases the cause of TTP may be related to an autoimmune mechanism. CVD and TTP have many clinical manifestations in common. Hemolytic anemia, thrombocytopenia, central nerve dysfunction, and renal dysfunction – the chief manifestations of TTP – often appear during the clinical course of SLE. Moreover, ANAs have been found in the sera of some patients with TTP.[11] Thus, it can be difficult to distinguish TTP from CVD.

We could not establish a diagnosis of SLE in this case because only two of the 1982 American Rheumatism Association revised criteria for SLE[12] (positive ANA assay and proteinuria) appeared during the clinical course. Subsequently, many burr and helmet cells in peripheral blood smears led us to diagnose TTP complicating primary SS with CrGN and MN. The renal histological features of glomeruli containing no hyaline thrombi may be due to the renal biopsy having been performed before the onset of TTP. Early diagnosis and treatment by plasma exchange has improved the poor prognosis of TTP[4]; therefore, we must be aware that the diagnosis of TTP may be delayed because of difficulty distinguishing TTP from CVD in some cases.

Renal involvement is often seen in patients with primary SS. Tubulointerstitial nephritis is the most frequent renal complication, but quite a few patients have glomerulonephritis.[13] Membranoproliferative glomerulonephritis has been shown in glomerular lesions with primary SS, but cases associated with CrGN are rare.[13,14] Renal involvement with primary SS was shown in almost all cases at an early stage, and it was occasionally preceded by dry signs.[14] The prognosis for patients with renal involvement is poor.[14] Although purpura, decreased C4, and cryoglobulinemia are strong predictors of glomerulonephritis in patients with primary SS,[15] CrGN associated with SS was almost always related to ANCA.[16–18] Glomerulonephritis in this case must have been caused by circulating IC because of the hypocomplementemia, increased circulating IC, IC deposition in mesangial matrix and subepithelium, and the absence of ANCA, anti-GBM antibody, and cryoglobulin in sera. However, a relation between CrGN with primary SS and IC has never been reported.

Crescentic glomerulonephritis and MN with primary SS is rare. Tatsumi et al.[19] reported a primary SS patient with CrGN and MN related to IC, similar to the present case, but TTP was not shown in their case. Fleuren et al.[20] demonstrated that ICs formed under conditions of antigen excess can deposit in the mesangium, whereas membranous localization of IC increased under conditions of antibody excess in rat kidney. Koyama et al.[21] showed that ICs were deposited mainly in the subendothelial side of the GBM and the mesangium in lupus nephritis patients with high-avidity antibodies. On the other hand, in the group with low-avidity antibodies, IC was localized on the subepithelial side of the GBM. They also showed that increasing avidity of antibodies causes deteriorating lupus nephritis, resulting in progression to CrGN from MN. These findings may indicate that ICs might have been complex or that alteration of antibody avidity developed during the clinical course in the present case.

Various causes of TTP have been reported. vWF-cleaving protease has now been purified, and its cDNA sequencing identified the enzyme as a metalloprotease.[22–24] Furlan et al.[5] and Tsai and Lian[6] showed that TTP is caused by a deficiency of plasma vWF-cleaving protease, and the autoantibody to vWF-cleaving protease was found in most, but not all, of these patients. These findings were significant because they clarified the role of vWF abnormalities, which had previously been suggested as a possible cause of TTP. However, antibody against vWF-cleaving protease was not shown in the sera of all patients with TTP, and TTP with unusually large vWF multimers has been reported in a small number of patients. It is not yet known if the autoantibody to vWF-cleaving protease is the main cause of TTP with CVD. Although we did not measure the autoantibody to

vWF-cleaving protease, unusually large vWF multimers were never seen in the plasma of the present case. This finding indicates that an association between vWF abnormalities and the TTP was unclear. Further systemic and detailed analysis of the autoantibody may clarify its physiological and clinical importance.

Human immunodeficiency virus (HIV)- and bacteria-derived endotoxins have been shown to be a cause of infection-associated TTP,[3] but TTP secondary to other infections is rare. In the present case, no infection was suggested as the cause of TTP because the patient was HIV-negative and there was no elevated endotoxin level in her serum, no manifestation of upper or lower respiratory tract infection, and no digestive tract symptoms such as diarrhea, preceding the development of TTP.

Thrombotic thrombocytopenic purpura complicating SS is rare. A review of the literature revealed six other such cases (Table 1).[8,25–27] Three (patients 1, 5, 7 in Table 1) of the total seven cases of TTP complicating SS (including ours) had cellular infiltration or immunological findings in the glomeruli. All three patients had a rapidly fatal course despite plasma exchange. Two other cases (patients 2 and 3) in whom PE was initiated had a relapse of their TTP. Two of them improved: one after repeated PE[8]and the other after corticosteroid and immunosuppressive treatment in addition to PE.[26] Most patients with TTP have a single acute episode after successful therapy. Relapsing and chronic forms of TTP are unusual.[28] These findings suggested that TTP with SS, especially cases with pathological findings of glomerulonephritis, are difficult to cure by the standard therapy of PE alone. Some additional treatment may be necessary for TTP with SS. The pathogenesis of TTP with SS may be different from that of primary TTP responding successfully to PE.

Table 1. Comparison of reported patients with TTP complicating Sjögren's syndrome

Pt.	Age/ sex	SS disease duration	Associated diseases	Immunological findings	Renal pathology	Treatment	Outcome	Reference
1	62/F	3 Months	Polymyositis, Interstitial pneumonia	Anti-SS-A antibody(+) ANA 5120 ×	1) Hyaline thrombi in arterioles and glomerular capillaries 2) Subendothelial deposits, onion-peeled fibrosis in arteries and arterioles 3) IgM deposits in glomerular capillaries 4) C1q and C3 deposits in small renal arteries	PE	Death	Noda et al.[25]
2	52/F	Not previously diagnosed	–	Anti-SS-A antibody(+)	–	PE repeated	3 short relapses, recovery	Schattner et al.[8]
3	54/F	3 years	Hypothyroidism	Anti-SS-A antibody(+) ANA 160 ×	–	PE PSL 100 mg/day CPA 150 mg/day	1 relapse, recovery	Campbell et al.[26]
4	49/F	Diagnosed at autopsy	RA, bacterial pneumonia	–	Hyaline thrombi in arterioles and glomerular capillaries	Transfusion	Death	Steinberg et al.[27]
5	51/F	7 years	RA	RF(+)	Hypercellular in glomeruli	–	Death	Steinberg et al.[27]
6	64/F	21 years	Multiple metastasis reticulum cell sarcoma, Sepsis	–	Hyaline thrombi in arterioles and glomerular capillaries	–	Death	Steinberg et al.[27]
7	75/F	2 months	–	Anti-SS-A antibody(+) Anti-SS-B antibody(+) ANA > 1280 ×	1) CrGN and MN 2) IgG and C3 deposits in glomerular capillaries 3) IC deposits in mesangial matrix and subepithelium	PE, PI, PGI_2 Steroid pulse	Death	Present case

ANA, antinuclear antibody; CPA, cyclophosphamide; CrGN, crescentic glomerulonephritis; MN, membranous nephropathy; PE, plasma exchange; PI, plasma infusion; PGI_2, prostaglandin I_2; PSL, prednisolone; RA, rheumatoid arthritis; RF, rheumatoid factor; SS, Sjögren's syndrome; TTP, thrombotic thrombocytopenic purpura

It has been shown in vitro that TTP patients' sera can cause immune destruction of human cultured endothelial cells, and their plasma is capable of causing spontaneous aggregation of normal human platelets.[29] Feldman et al.[30] reported faint deposits of IgG in the subendothelial space of arteries and arterioles, in the mesangium, and along the glomerular capillary wall in renal tissues from patients with TTP. Furthermore, the endothelium was detached from the GBM, and the subendothelial space was widened and occupied by electron-lucent material.[31] Noda et al.,[25] who reported a case (patient 1 in Table 1), showed diffuse granular deposits of IgM, fibrinogen, and C1q along the capillary walls of the kidney. They stated that in their case IC seemed to be a causative factor of TTP. In our case, IgG and C3 were seen in glomerular capillaries, and immune deposits were shown in the mesangial matrix and subepithelium. Therefore, it is possible that immune complexes were also a causative agent of TTP in our patient.

Conclusions

We reported a case of thrombotic thrombocytopenic purpura complicating Sjögren's syndrome accompanied by crescentic glomerulonephritis and membranous nephropathy. For the patient who has Sjögren's syndrome with renal involvement, the prognosis is poor. Our patient died within 3 months after disease onset, with no remission, despite intensive therapy including steroid pulse therapy and plasma exchange.

References

1. Moschcowitz E. Hyaline thrombosis of the terminal arterioles and capillaries: a hitherto undescribed disease. Proc N Y Pathol Soc 1924;24:21–4.
2. Moake JL. Studies on the pathophysiology of thrombotic thrombocytopenic purpura. Semin Hematol 1997;34:83–9.
3. Elliott MA, Nichols WL. Thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. Mayo Clin Proc 2001;61:1154–62.
4. Ruggenenti P, Noris M, Remuzzi G. Thrombotic microangiopathy, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura. Kidney Int 2001;60:831–46.
5. Furlan M, Robles R, Galbusera M, Remuzzi G, Kyrle PA, Brenner B, et al. Von Willebrand factor-cleaving protease in thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. N Engl J Med 1998;339:1578–84.
6. Tsai HM, Lian EC. Antibodies to von Willebrand factor-cleaving protease in thrombotic thrombocytopenic purpura. N Engl J Med 1998;339:1585–94.
7. Caramaschi P, Riccetti MM, Pasini AF, Savarin T, Biasi D, Todeschini G. Systemic lupus erythematosus and thrombotic thrombocytopenic purpura: report of three cases and review of the literature. Lupus 1998;7:37–41.
8. Schattner A, Friedman J, Klepfish A. Thrombotic thrombocytopenic purpura as an initial presentation of primary Sjögren's syndrome. Clin Rheumatol 2002;21:57–9.
9. Di-Pietro G, Menicucci A, Venturini S, Avanzi G. A case of thrombotic thrombocytopenic purpura preceding onset of systemic lupus erythematosus. J Clin Apheresis 1996;11:51–2.
10. Towheed TE, Anastassiades TP, Ford SE, Ford PM, Lee P. Thrombotic thrombocytopenic purpura as an initial presentation of limited systemic sclerosis. J Rheumatol 1999;26:1613–6.
11. Brunner HI, Freedman M, Silverman ED. Close relationship between systemic lupus erythematosus and thrombotic thrombocytopenic purpura in childhood. Arthritis Rheum 1999;42:2346–55.
12. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–7.
13. Goules A, Masouridi S, Tzioufas AG, Ioannidis JP, Skopouli FN, Moutsopoulos HM. Clinically significant and biopsy-documented renal involvement in primary Sjögren's syndrome. Medicine 2000;79:241–9.
14. Bossini N, Savoldi S, Franceschini F, Mombelloni S, Baronio M, Cavazzana I, et al. Clinical and morphological features of kidney involvement in primary Sjögren's syndrome. Nephrol Dial Transplant 2001;16:2328–36.
15. Skopouli FN, Dafni U, Ioannidis JP, Moutsopoulos HM. Clinical evolution, and morbidity and mortality of primary Sjögren's syndrome. Semin Arthritis Rheum 2000;29:296–304.
16. Kamachi M, Migita K, Tominaga M, Ichinose Y, Nakamura H, Origuchi T, et al. Sjögren's syndrome complicated by MPO-ANCA positive crescentic glomerulonephritis. Nephrol Dial Transplant 1999;14:1033–4.
17. Hernandez JL, Rodrigo E, De Francisco AL, Val F, Gonzalez-Macias J, Riancho JA. ANCA-associated pauci-immune crescentic glomerulonephritis complicating Sjögren's syndrome. Nephrol Dial Transplant 1996;11:2313–5.
18. Bottinger EP, Niles JL, Collins AB, McCluskey RT, Arnaout MA. Antineutrophil cytoplasmic autoantibody-associated vasculitis presenting as Sjögren's syndrome. Arthritis Rheum 1992;35:1373–6.
19. Tatsumi H, Tateno S, Hiki Y, Shigematsu H, Kobayashi Y. Crescentic glomerulonephritis associated with membranous nephropathy in a case with primary Sjögren's syndrome. Nephrol Dial Transplant 1998;13:2624–7.
20. Fleuren GJ, van den Lee R, Greben HA, Van Damme BJ, Hoedemaeker PJ. Experimental glomerulonephritis in the rat induced by antibodies directed against tubular antigens. IV. Investigations into the pathogenesis of the model. Lab Invest 1978;38:496–501.
21. Koyama A, Narita M, Tojo S. Antibody avidity for native DNA in lupus nephritis. Contrib Nephrol 1977;4:72–82.
22. Gerritsen HE, Robles R, Lammele B, Furlan M. Partial amino acid sequence of purified von Willebrand factor-cleaving protease. Blood 2001;98:1654–61.
23. Fujikawa K, Suzuki H, McMullen B, Chung D. Purification of human von Willebrand factor-cleaving protease and its identification as a new member of the metalloproteinase family. Blood 2001;98:1662–6.
24. Zheng X, Chung D, Takamiya TK, Majerus EM, Sadler JE, Fujikawa K. Structure of von Willebrand factor-cleaving protease (ADAMTS 13), a metalloprotease involved in thrombotic thrombocytopenic purpura. J Biol Chem 2001;276:41059–63.
25. Noda M, Kitagawa M, Tomoda F, Iida H. Thrombotic thrombocytopenic purpura as a complicating factor in a case of polymyositis and Sjogren's syndrome. Am J Clin Pathol 1990;94:217–21.
26. Campbell GN, Gallo JH. Relapsing thrombotic thrombocytopenic purpura (TTP) in Sjogren's syndrome. Aust N Z J Med 1998;28:214.
27. Steinberg AD, Green WT Jr, Talal N. Thrombotic thrombocytopenic purpura complicating Sjogren's syndrome. JAMA 1971;215:757–61.
28. Shumak KH, Rock GA, Nair RC. Late relapses in patients successfully treated for thrombotic thrombocytopenic purpura: Canadian Apheresis Group. Ann Intern Med 1995;122:569–72.
29. Burns ER, Zucker-Franklin D. Pathologic effects of plasma from patients with thrombotic thrombocytopenic purpura on platelets and cultured vascular endothelial cells. Blood 1982;60:1030–7.
30. Feldman JD, Mardiney MR, Unanue ER, Cutting H. The vascular pathology of thrombotic thrombocytopenic purpura: an immunohistochemical and ultrastructural study. Lab Invest 1966;15:927–46.
31. Remuzzi G, Ruggenenti P, Bertani T. Thrombotic microangiopathy. In: Tisher CC, Brenner BM, editors. Renal pathology: with clinical and functional correlations. 2nd ed. Philadelphia: Lippincott; 1994. p. 1162–4.