Systemic vasculitis in a patient with rhupus syndrome

O. Zengin[1], M.E. Onder[1], M.A. Sarica[2], I.H. Turkbeyler[3], G. Kimyon[1], Z.H. Demir[4], H. Yildiz[5], B. Kisacik[1], A.M. Onat[1]

[1]Department of Rheumatology, Gaziantep University, Faculty of Medicine, Gaziantep, Turkey;
[2]Department of Radiology, Kahramanmaraş Sutcu Imam University, Faculty of Medicine, Kahramanmaraş, Turkey;
[3]Department of Geriatrics, Gaziantep University, Faculty of Medicine, Gaziantep, Turkey;
[4]Center for Cognitive Neurology, New York University School of Medicine, New York, NY, USA;
[5]Department of Internal Medicine, Gaziantep University, School of Medicine, Gaziantep, Turkey

SUMMARY

Rhupus is a rare syndrome characterized by overlap of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Previous reports mentioned that rhupus patients have prominent RA associated clinical manifestations and only mild organic damage related to SLE. Progressive or life-threatening manifestations are rare in rhupus patients. Our patient diagnosed as rhupus was a young women, presented with multi-organ involvement of systemic vasculitis. Rheumatologists should be aware of possibility that rhupus may be accompanied by progressive or life-threatening conditions such as vasculitis.

Key words: *Rhupus; vasculitis; systemic lupus erythematosus; rheumatoid arthritis.*

Reumatismo, 2015; 67 (4): 161-164

Non-commercial use only

INTRODUCTION

Systemic lupus erythematosus (SLE) that is co-morbid with rheumatoid arthritis (RA) is known as *rhupus syndrome* (1). The overlap of RA and SLE was first described by Schur, in 1971, as *rhupus* (2). Rhupus syndrome is a rare clinical condition; only a few cases have been reported. The syndrome constitutes 0.01-2% of all systemic rheumatic disease (3). Vasculitis reported in 10-40% of SLE patients, usually as small vessel vasculitis. Vasculitis also seen in RA, but rheumatoid vasculitis is an unusual complication of long-standing RA. Here, we report the case of a young female with fulminant vasculitis and Rhupus syndrome; this is first example of such a disease overlap.

CASE REPORT

A 28-year-old female patient was admitted complaining of pain in both ankles, both knees, and the metacarpophalangeal (MCP) and wrist joints, as well as bluish discoloration of the toes. She reported that the pain and swelling in both her hand and feet joints had been of almost 1 year in duration, and that the Raynaud's phenomenon in the toes had become especially notable over the past 10 days. She had no comorbidity. On physical examination, the dorsalis pedis pulses were bilaterally weak; both ankles, knees, and wrists, and all MCP joints, were painful; and swelling and alopecia were evident. The laboratory data were: hemoglobin 11.2 g/dL, mean corpuscular volume 88 fL, mean corpuscular hemoglobin 30.5 pg, leukocytes 12,500/mm³, eosinophils 120/mm³ (normal range 100-450/mm³), platelets 512,000/mm³, urea 36 mg/dL, creatinine 0.5 mg/dL, aspartate aminotransferase 37 IU/L, alanine aminotransferase 48 IU/L, and C-reactive protein 168 mg/dL (normal range 0-5 mg/dL). The erythrocyte sedimentation rate was 140 mm/h (normal range 1-20 mm/h). The rheumatoid factor (RF) level was 256 IU/mL (normal range 0-15 IU/mL) and the anti-citrullinated cyclic peptide antibody (anti-CCP) level 123 IU/mL (normal range 0-15 IU/mL). The serum was positive for antinuclear antibody (ANA) (titer 1:320; normal <1/80), anti-dsDNA antibody (titer >1:300; normal 0-20); and anti

Corresponding author
Orhan Zengin
Department of Rheumatology,
Faculty of Medicine
Gaziantep University, Gaziantep,
TR-27310, Turkey
E-mail: drorhanzengin@gmail.com

SS-A antibody (45 U/mL; normal 0-15 U/mL). The level of complement component 3 (C3) was 0.01 g/L (normal 0.9-1.8 g/L) and that of complement component 4 (C4) 0.002 g/L (normal 0.1-0.4 g/L). The serum was negative for perinuclear anti-neutrophil cytoplasmic antibodies and cytoplasmic anti-neutrophil cytoplasmic antibodies. Antiphospholipid antibodies including anti-cardiolipin antibody, anti-beta 2 glycoprotein I antibody, and lupus anticoagulant were within normal ranges. The urine protein level was 860 mg/day. The characteristic radiological changes included narrowing of the joint lines, cysts, and periarticular osteoporosis. The serological data (high-level RF and anti-CCP positivity) and the symmetrical polyarthritis were suggestive of RA. However, the low serum C3, C4, and ANA levels; the anti-dsDNA and anti-SS-A positivity; and the alopecia and proteinuria, were suggestive of SLE. Angiography demonstrated multiple aneursymatic dilatations of celiac artery and branches (Figure 1). Multiple aneursymatic dilatations of superior mesenteric artery were also demonstrated with angiography (Figure 2). The patient was diagnosed with Rhupus syndrome accompanied by systemic vasculitis and prescribed 1 g of methylprednisolone intravenously, daily for three days. Cyclophosphamide 500 mg weekly was added. In the third week of treatment, she developed chest pain. The cardiac biomarkers were elevated and echocardiography revealed global hypokinesia of the left ventricle with an ejection fraction of 25%. Coronary angiography revealed widespread aneurysmatic dilatations in all three epicardial coronary arteries and saccular aneurysms in the right coronary artery. Rituximab therapy was planned but the patient died before such therapy could commence, because of her heart problems.

DISCUSSION

We describe a patient with Rhupus syndrome accompanied by systemic vasculitis. This case is remarkable, being the first ever reported. Rhupus is a particular syndrome featuring an overlap of RA and SLE and characteristically manifests with more RA-associated and less SLE-associated damage (4). Progressive or life-threatening manifestations are rare in Rhupus patients. The prognosis of rhupus syndrome often depends on the severity of damage to the vital organs, but is typically better than that of SLE but poorer than that of RA. Very little information is available on treatment of rhupus syndrome. Possible treatments include conventional disease-modifying antirheumatic drugs followed, in some resistant cases, by rituximab and abatacept (3). Commonly, the vital organs are involved,

Non-commercial use only

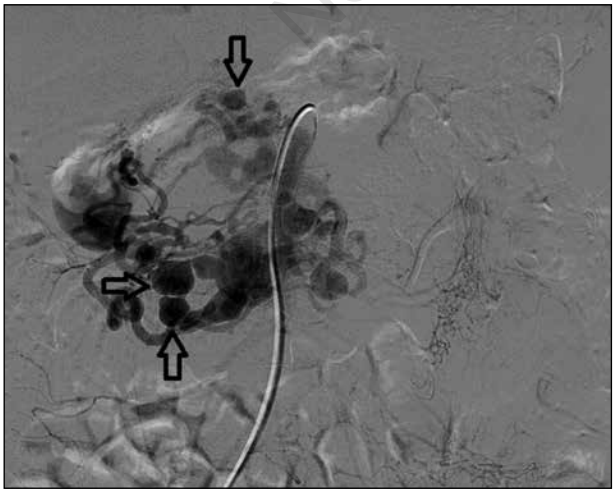

Figure 1 - Angiography demonstrated multiple aneurysmatic dilatations of celiac artery and branches.

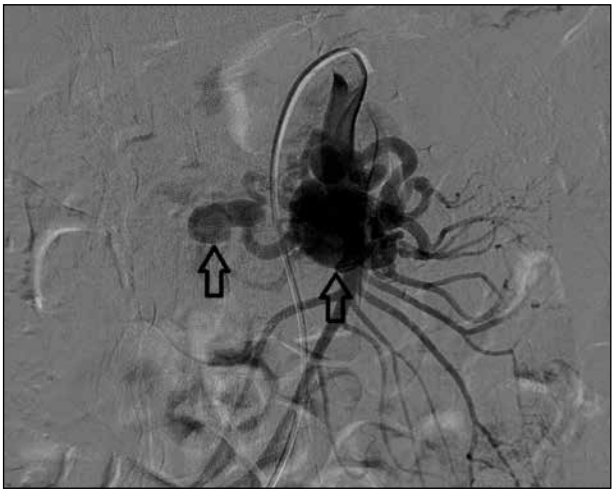

Figure 2 - Angiography demonstrated multiple aneurysmatic dilatations of superior mesenteric artery.

as in our patient. This, combined with the vasculitis, rendered prognosis poor. We initiated pulse steroid and cyclophosphamide, but the treatment outcome was poor. Thus, we decided to add rituximab, but the patient died before such therapy could commence.

The vascular lesions of SLE are commonly termed lupus vasculopathy; this is a typical vasculitis associated with inflammation and vascular wall necrosis. Vasculitis is reported in 10-40% of patients, more often in females (80%) than males (5). SLE is usually associated with small-vessel vasculitis. Medium- and large-vessel vasculitis is distinctly uncommon in SLE; there are only a few case reports (6). Suzuki et al. reported a case of cerebral and systemic necrotizing vasculitis developing during pregnancy in an SLE patient (7). Grimbacher reported a female patient who developed gastrointestinal vasculitis and who was successfully treated with cyclophosphamide (8). Our patient was female, suggesting that she had SLE-related vasculitis. But involvement of the medium and large vessels is not typical of SLE vasculitis.

Vasculitis in RA patients has an heterogeneous clinical presentation, including skin disorders, neuropathy, eye symptoms, and visceral infarction (9, 10). The vascular lesions of RA are mostly asymptomatic but may occasionally manifest severely (11). The cause of rheumatoid vasculitis (RV) is unknown but, given the prominence of immune system components and pathological changes in the involved blood vessels, an autoimmune process may be in play (10). Systemic RV typically occurs in patients with long-standing, seropositive, erosive nodular RA, and is associated with a severe disease course and extra-articular manifestations. Blood vessels of any size, from the aorta to capillaries, may be involved, and organ involvement is widespread. The prognosis of systemic RV is generally thought to be poor (12). Ashima performed a case control study on 86 patients and found that cutaneous vasculitis was the most common presentation, followed by vasculitic neuropathy. Also, a long duration of disease, male gender, smoking, and rheumatoid nodules, were associated with vasculitis (9). Our patient was female, her disease duration was short (1 year), and she lacked rheumatoid nodules. She also did not exhibit neuropathy or a skin disease. However, her seropositivities, the involvement of the aorta and large vessels, and the widespread multi-organ involvement, were compatible with RV. She lacked any known risk factor but developed serious vasculitis. Therefore, SLE may have contributed to disease severity.

Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that typically affects the medium-sized muscular arteries, particularly those of the viscera, kidneys, and soft tissue (13). Visceral angiography may be performed when PAN is highly suspected and a histological diagnosis of vasculitis cannot be made, or when the predominant symptoms are suggestive of abdominal, renal, or cardiac involvement (14). Therefore, we performed angiography to allow a differential diagnosis. Aneurisms were evident, but they were not of the form typical of PAN. Also, the clinical and laboratory findings differed from those of PAN. The tissues most frequently affected in PAN (the peripheral nerves and the skin) were not involved in our patient. In addition, she had no fever, no weight loss, no abdominal pain; and her blood pressure was not elevated. These symptoms are common in PAN patients. Our patient was positive for markers of SLE and RA, but negative for hepatitis B. Such characteristics allowed us to eliminate PAN from consideration.

Vasculitis may develop over the long term in RA and SLE patients. However, systemic vasculitis has not previously been described in a patient with Rhupus. In 2010, Wang et al. described a Rhupus case that progressed to diffuse encephalopathy caused by microangiopathy. The 37 year-old female patient developed epileptic seizures. Magnetic resonance imaging revealed diffuse hyperintensity; the patient was successfully treated with methylprednisolone (15). In the cited case, Rhupus presented as only brain vasculitis. In our case, the vasculitis was multi-organ in nature.

Traditionally, the vasculitides are defined as a group of clinical and pathological enti-

Non-commercial use only

ties characterized by inflammatory cell infiltration and necrosis of blood vessel walls. The conditions may be primary in nature, involving large, medium, and/or small vessels; or secondary, associated with infection, malignant and/or connective tissue disease, or exposure to certain medications. Our patient had no sign of malignancy or infection clinically, radiologically, or upon laboratory evaluation. She had no history of exposure to drugs (*e.g*., ergot, cocaine) that mimic vasculitis. Thus, we excluded all other causes of vasculitis. Our patient was diagnosed with the SLE/RA overlap syndrome, termed Rhupus, and we suggest that vasculitis in our patient is a complication of Rhupus.

CONCLUSIONS

Rhupus syndrome is a particular form of overlap of RA and SLE. Our patient diagnosed as rhupus developed vasculitis. We evaluated all possible causes of her clinical manifestations on admission. We excluded vasculitis that was paraneoplastic in nature, or caused by an infection or drug use. We report on the development of medium-vessel vasculitis in a Rhupus patient. No similar case has ever been reported. Patients with rhupus must be carefully monitored; they are at risk of vasculitis.

Conflict of interest: the authors declare that they have no conflict of interest.

Non-commercial use only

REFERENCES

1. Seo SR, Lee SJ, Park DJ, et al. Successful treatment using cyclosporine in a patient with rhupus complicated by aplastic anemia: a case report and review of the literature. Clin Exp Rheumatol. 2011; 29: 708-11.
2. Schur PH. Systemic lupus erythematosus. In: Beeson PB, McDermott W, eds. Cecil-loeb textbook of medicine. 13th ed. Philadelphia: WB Saunders. 1971; 821.
3. Shovman O, Langevitz P, Shoenfeld Y. Rhupus; unusual presentations. Clin Rheumatol. 2015; 34: 2041-6.
4. Li J, Wu H, Huang X, et al. Clinical analysis of 56 patients with rhupus syndrome: manifestations and comparisons with systemic lupus erythematosus: a retrospective case-control study. Medicine (Baltimore). 2014; 93: e49.
5. Cieslik P, Hrycek A, Klucinski P. Vasculopathy and vasculitis in systemic lupus erythematosus. Pol Arch Med Wewn. 2008; 118: 57-63.
6. Kumar N, Choudhary N, Agarwal G, et al. Extensive medium-vessel vasculitis with SLE: an unusual association. J Clin Rheumatol. 2007; 13: 140-2.
7. Suzuki Y, Kitagawa Y, Matsuoka Y, et al. Severe cerebral and systemic necrotizing vasculitis developing during pregnancy in a case of systemic lupus erythematosus. J Rheumatol. 1990; 17: 1408-11.
8. Grimbacher B, Huber M, von Kempis J, et al. Successful treatment of gastrointestinal vasculitis due to systemic lupus erythematosus with intravenous pulse cyclophosphamide: a clinical case report and review of the literature. Br J Rheumatol. 1998; 37: 1023-8.
9. Makol A, Crowson CS, Wetter DA, et al. Vasculitis associated with rheumatoid arthritis: a case-control study. Rheumatology (Oxford). 2014; 53: 890-9.
10. Cojocaru M, Cohocaru IM, Chico B. New insight into the rheumatoid vasculitis. Rom J Intern Med. 2015; 53: 128-32.
11. Cestelli V, Spinella A, Campomori F, et al. Large vessel vasculitis occurring in rheumatoid arthritis patient under anti-TNF therapy. Case Rep Med. 2014; 2014: 624184.
12. Ntatsaki E, Mooney J, Scott DG, Watts RA. Systemic rheumatoid vasculitis in the era of modern immunosuppressive therapy. Rheumatology (Oxford). 2014; 53: 145-52.
13. Forbess L, Bannykh S. Polyarteritis nodosa. Rheum Dis Clin N Am. 2015; 41: 33-46.
14. Hernandez-Rodriguez J, Alba MA, Prieto-Gonzalez S, Cid MC. Diagnosis and classification of polyarteritis nodosa. J Autoimmun. 2014; 48-49: 84-9.
15. Wang J-G, Tang H-H, Tan C-Y, et al. Diffuse lupus encephalopathy in a case of rhupus syndrome. Rheumatol Int. 2010; 30: 961-3.