J Microbiol Immunol Infect
2005;38:296-299

Second-degree atrioventricular block as an early manifestation of adult systemic lupus erythematosus

An-Ping Huo[1], Kang-Cheng Su[2], Hsien-Tzung Liao[1], Chung-Tei Chou[1], Hsiao-Ning Chang[1]

[1]Section of Allergy, Immunology, and Rheumatology, Department of Medicine and [2]Department of Chest Medicine, Taipei Veterans General Hospital and National Yang-Ming University School of Medicine, Taipei, Taiwan

Received: February 4, 2004 Revised: March 1, 2004 Accepted: September 15, 2004

Second-degree atrioventricular (AV) block had not been reported as an early manifestation of adult systemic lupus erythematosus (SLE). An 18-year-old woman of SLE presented with asymptomatic second-degree AV block with 2:1 conduction block on electrocardiogram (ECG) during admission. Serologic tests were negative for anti-Sjögren's syndrome A (anti-SS-A/Ro) and anti-SS-B/La antibodies, but positive for anti-ribonuclearprotein antibodies. Her abnormal ECG completely resolved soon after high-dose intravenous methylprednisolone infusion, and she was maintained successfully with a low dose of oral steroid. The possible pathogenesis of this complication is discussed. Follow-up with periodical ECG is recommended for adult lupus patients to screen for possible conduction system involvement, and treatment should be started as soon as possible.

Key words: Heart block, ribonuclearprotein antigen, SS-A antibodies, systemic lupus erythematosus

Atrioventricular (AV) conduction defect is a rare manifestation of adult systemic lupus erythematosus (SLE). Two cases of second-degree AV block have been previously reported. Both presented late in the course of underlying SLE and progressed to advanced AV conduction defect within 1 day [1,2]. But second-degree AV block has not been reported as an initial condition in adult SLE. We report a case of transient second-degree AV block as the early manifestation of adult SLE. The condition resolved completely after high-dose steroid treatment. The possible mechanism for this manifestation is also discussed.

Case Report

An 18-year-old woman had been in robust health, without any obvious family history of cardiovascular disease. She began suffering from fever without chills, malar rash, polyarthralgia, oral ulcer, and photosensitivity that persisted for more than 10 days in early November 2003, and was admitted to a local hospital. She was treated for a urinary tract infection with intravenous cefuroxime 1500 mg 8-hourly from November 19 to 25, 2003. During that admission, laboratory studies disclosed proteinuria, with 24-h urinary protein 4.86 g/day and serum albumin 2.3 mg/dL. Creatinine clearance (CCr) was 59.4 mL/min; complement factors C3/C4 30/11.1 mg/dL; antinuclear antibodies (ANA) 1:320, speckle pattern; Coomb's test (+); and anti-ds-DNA 640 IU/mL. Due to a suspicion of SLE with lupus nephritis, she was transferred to our ward for further management on November 25, 2003.

Physical examination disclosed mild swelling in the bilateral knees, mild pitting edema in the bilateral lower legs, and a regular heart beat without murmur. Electrocardiogram (ECG) at admission showed a normal sinus rhythm. The blood test rendered the following results: hemoglobulin 10.9 g/dL; hematocrit 31.8%; mean corpuscular volume 85.4 fL; leukocyte count 3900/mm^3; lymphocyte count 663/mm^3; platelet count 124,000/mm^3; erythrocyte sedimentation rate 23 mm/h C-reactive protein 0.705 mg/dL; serum albumin 2.2 mg/dL; blood urea nitrogen/Cr, 11/0.7 mg/dL; and creatinine kinase (CK), 31 U/L. The serologic test showed low C3/C4 (18.1/4.45 mg/dL); negative rheumatoid factor; positive ANA (1:320, speckle pattern), anti-ribonuclearprotein (anti-RNP) antibodies, but negative anti-Sjögren's syndrome A antibodies (anti-SS-A/Ro), anti-SS-B/La, and immunoglobulin M (IgM) anti-cardiolipin antibodies. Additional findings showed direct/indirect Coomb's test (+)/(-); activated partial thromboplastin time (aPTT) 42.3 s (control 30.0 s); normal mixed aPTT at 0 and 2 h; lupus

Corresponding author: Hsiao-Ning Chang, Section of Allergy, Immunology, and Rheumatology, Department of Medicine, Taipei Veterans General Hospital, 201 Sec. 2, Shipai Road, Taipei 112, Taiwan.
E-mail: hnchang@vghtpe.gov.tw

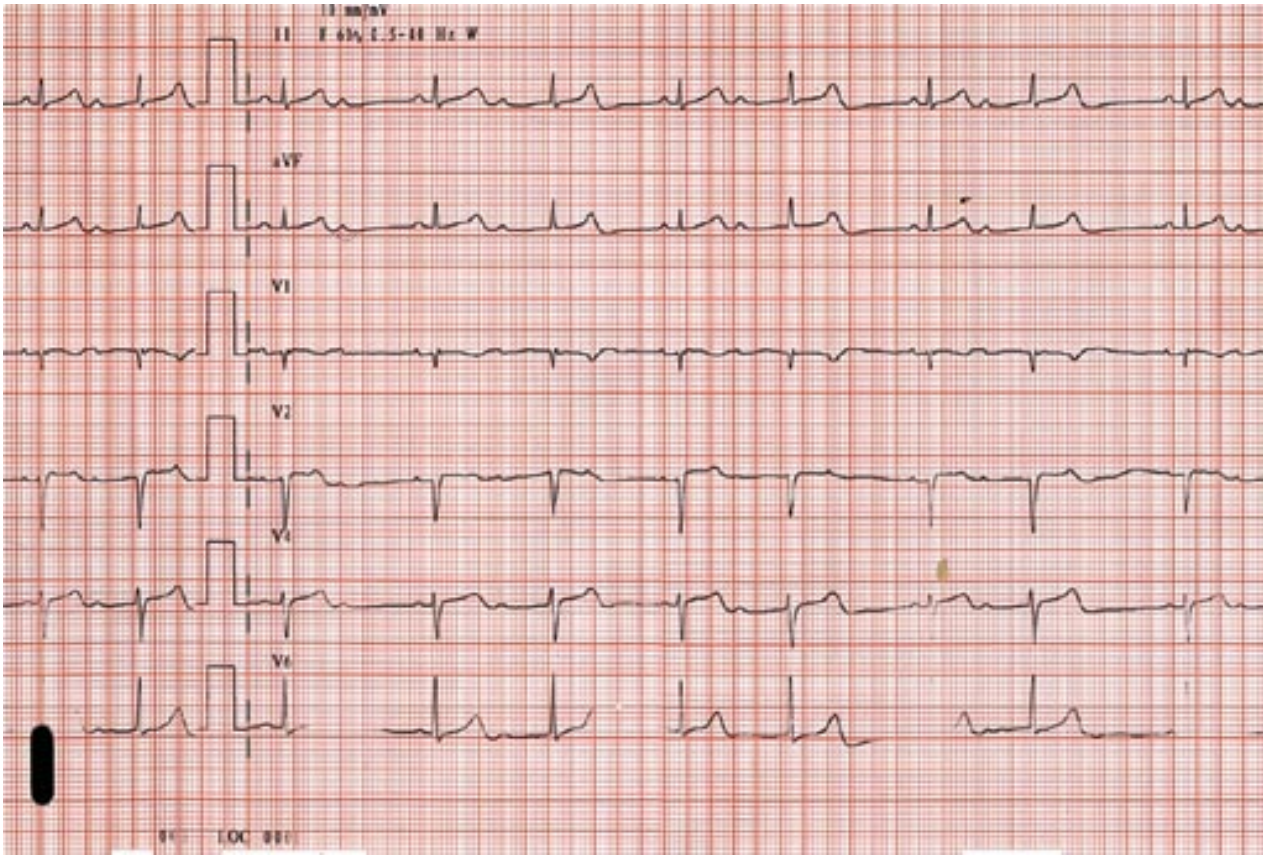

Fig. 1. 2:1 second-degree artioventricular block with constant PR interval.

anticoagulant negative; triiodothyronine 82.81 ng/dL; free thyroxine 0.94 ng/dL; thyroid-stimulating hormone 3.416 μIU/mL; positive red blood cell cast on routine urine examination; 24-h urinary protein 2.04 g/day; and CCr 62 mL/min. SLE with lupus nephritis was diagnosed, and a renal biopsy was suggested. Incidentally, asymptomatic bradycardia (heart rate 45-52/min) was noted just before performing the renal biopsy on December 2, 2003. ECG showed a 2:1 AV block with a ventricular response of 40-50 beats per min and an atrial rate of 80-100 beats per min (constant PR interval 0.12 s, in favor of Mobitz type II) [Fig 1]. CK myoblobin fraction (CK-MB)/troponin-I sodium, potassium, and free calcium were checked immediately, and all these results were within normal ranges (CK 18U/L, CK-MB 1U/L, troponin-I: 0.04 ng/mL, sodium 135 mmoL/L, potassium 4.6 mmoL/L, free calcium 1.22 mmoL/L). Echocardiography was also performed, and no obvious abnormal findings were noted. Therefore, a renal biopsy was suspended, and a temporal pacemaker (TPM) was inserted immediately to prevent progression to complete AV block. High-dose intravenous methylprednisolone 800 mg/day was administered from December 3 to 5, 2003, and steroid therapy was then continued with oral prednisolone 30 mg/day. Fortunately, the heart rate returned to a normal sinus rhythm since December 6, 2003, and complete remission was noted since December 8, 2003. Due to stable vital signs in spite of 2:1 AV block, the TPM had never been activated, and was removed on December 9, 2003. She was discharged on December 23, 2003, under stable conditions after the steroid had been tapered to 20 mg/day, with outpatient follow-up.

Discussion

Pericarditis is the most common clinical manifestation of cardiac involvement in adult lupus patients. It typically presents with low voltage of the QRS complex, and diffuse ST-segment elevation and T wave inversion on the ECG, while AV conduction defect is uncommon. It is characterized by onset late in the course of the underlying disease, or development in patients taking hydroxychloroquine. Our review of the literature revealed 19 reported cases of AV conduction block in adult lupus patients [1-9]. Among the reported

conduction defects, only 2 were initially second-degree AV block and both of them late manifestations of the underlying disease that progressed to complete AV block within 1 day [1,2]. In addition, hydroxychloroquine-induced conduction defect was not excluded in 1 case [1], and myositis or myocarditis, which may also have contributed to the AV conduction defect, was also not excluded in the other [2]. Therefore, no adult patient with SLE-related second-degree AV block as an early manifestation had been reported.

AV conduction block is a frequent manifestation in neonatal lupus erythematosus, and the pathogenesis was considered to correlate with the presence of serum anti-SSA/Ro antibodies [10]. Deng et al demonstrated the presence of Ro (SS-A) antigen in the hearts of fetuses from normal mothers [11], and diffuse IgG stains of the myocardium in infants with congenital heart block also had been demonstrated by Litsey et al [12] and Taylor et al [13]. Our patient's serum was negative for anti-SS-A/Ro and anti-SS-B/La antibodies but positive for anti-RNP antibodies. High titers of anti-RNP antibodies have been shown to correlate with mixed connective tissue disease (MCTD) [14,15], and the most common cardiovascular involvement of patients with MCTD is pericarditis, which may also contribute to the conduction system dysfunction. Although our patient had a positive result for anti-RNP antibodies, no obvious evidence of MCTD or pericarditis was present. Among the previously reported 19 cases complicated with AV conduction block, 4 had positive results for both anti-SS-A/Ro and anti-RNP antibodies in the serum [1,2,5, 7], one for anti-SS-A/Ro antibodies alone [6], and another for anti-RNP antibodies alone [8], as did our patient. Whether anti-RNP antibodies or anti-SS-A/Ro antibodies play an important role in the pathogenesis of the AV conduction defect in adult SLE is uncertain due to the small reported number of cases.

James et al described 4 categories of abnormal histologic findings in the cardiac conduction system in adult SLE: 1) the presence of pericarditis; 2) arteriopathy; 3) endocardial reaction beneath the sinus node; and 4) abnormality of collagen in both the sinus node and the AV node [4]. Although there was no direct evidence or positive angiographic findings in our patient, the absence of anti-SS-A/Ro and anti-SS-B/La antibodies, the presence of anti-RNP antibodies without obvious evidence of MCTD, myocarditis or pericarditis, the sudden onset of second-degree AV block without the presentation of previous bundle branch block, and the dramatic improvement after intravenous methylprednisolone infusion, all suggest that this complication may have been due to reversible vasculitis or thrombosis involving the arteries supplying the sinoatrial node or AV node, not irreversible sinus node or AV node collagen degeneration.

Moffitt proposed that complete AV block might be the terminal event of conduction system involvement in adult SLE, which may be preceded by a bundle branch block [3]. Based on Moffitt's proposal and the clinical courses of the previous 2 case reports [1,2], whether the conduction block in our patient may progress to complete AV block if treatment is delayed is unknown. Routine ECG should be periodically performed in patients with SLE to screen for possible conduction system involvement, and treatment should be started as soon as possible.

References

1. Comin-Colet J, Sánchez-Corral MA, Alegre-Sancho JJ, Valverde J, Lòpez-Gòmez D, Sabaté X, et al. Complete heart block in an adult with systemic lupus erythematosus and recent onset of hydroxychloroquine therapy. Lupus 2001;10: 59-62.
2. Bilazarian SD, Taylor AJ, Brezinski D, Hochberg MC, Guarnieri T, Provost TT. High-grade atrioventricular heart block in an adult with systemic lupus erythematosus: the association of nuclear RNP (U1 RNP) antibodies, a case report, and review of the literature. Arthritis Rheum 1989;32:1170-4.
3. Moffitt GR Jr. Complete atrioventricular dissociation with Stokes-Adams attacks due to disseminated lupus erythematosus. Report of a case. Ann Intern Med 1965;63: 508-11.
4. James TN, Rupe CE, Monto RW. Pathology of the cardiac conduction system in systemic lupus erythematosus. Ann Intern Med 1965;63:402-10.
5. Maier WP, Ramirez HE, Miller SB. Complete heart block as the initial manifestation of systemic lupus erythematosus. Arch Intern Med 1987;147:170-1.
6. Martinez-Costa X, Ordi J, Barberá J, Selva A, Bosch J, Vilardell M. High grade atrioventricular heart block in 2 adults with systemic lupus erythematosus. J Rheumatol 1991;18: 1926-8.
7. Mevorach D, Raz E, Shalev O, Steiner I, Ben-Chetrit E. Complete heart block and seizures in an adult with systemic lupus erythematosus. A possible pathophysiologic role for anti-SS-A/Ro and anti-SS-B/La autoantibodies. Arthritis Rheum 1993;36:259-62.
8. Fonseca E, Crespo M, Sobrino JA. Complete heart block in an adult with systemic lupus erythematosus. Lupus 1994;3: 129-31.

9. Gómez-Barrado JJ, García-Rubira JC, Polo Ostáriz MA, Turegano Albarrán S. Complete atrioventricular block in a woman with systemic lupus erythematosus. Int J Cardiol 2002; 82:289-92.
10. Reed BR, Lee LA, Harmon C, Wolfe R, Wiggins J, Peebles C, et al. Autoantibodies to SS-A/La in infants with congenital heart block. J Pediatr 1983;103:889-91.
11. Deng JS, Bair LW Jr, Shen-Schwarz S, Ramsey-Goldman R, Medsger T Jr. Localization of Ro (SS-A) antigen in the cardiac conduction system. Arthritis Rheum 1987;30: 1232-8.
12. Litsey SE, Noonan JA, O'Connor WN, Cottrill CM, Mitchell B. Maternal connective tissue disease and congenital heart block: demonstration of immunoglobulin in cardiac tissue. N Engl J Med 1985;312:98-100.
13. Taylor PV, Scott JS, Gerlis LM, Esscher E, Scott O. Maternal antibodies against fetal cardiac antigens in congenital complete heart block. N Engl J Med 1986;315:667-72.
14. Sharp GC, Irvin WS, Tan EM, Gould RG, Holman HR. Mixed connective tissue disease—an apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). Am J Med 1972;52: 148-59.
15. Sharp GC, Irvin WS, May CM, Holman HR, McDuffie FC, Hess EV, et al. Association of antibodies to ribonucleoprotein and Sm antigens with mixed connective-tissue disease, systemic lupus erythematosus and other rheumatic diseases. N Engl J Med 1976;295:1149-54.