Anti Ro/SSA Positive Undifferentiated Connective Tissue Disease Mother with a Newborn with Complete Congenital Heart Block: A Case Report†

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Abstract

An association between complete congenital heart block (CCHB) and anti-Ro/SSA antibody is well recognized but has never been reported in Thailand. We report here a 37-year-old female who was admitted because of massive epistaxis secondary to immune thrombocytopenia. She had given birth to a child with CCHB 2 years previously, when she was healthy. Antinuclear antibody and anti-Ro/SSA were positive in her sera, but were negative in her son. The relationship between anti-Ro/SSA antibody and outcome of mothers with infants with CCHB is reviewed.

Anti-Ro/SSA antibody is found in many connective tissue diseases, including systemic lupus erythematosus (SLE), Sjögren's syndrome, rheumatoid arthritis, scleroderma and polymyositis[1]. It is usually found in association with anti-La/SSB antibody. Many clinical syndromes associated with anti-Ro/SSA have been established, these include subacute cutaneous lupus erythematosus (SCLE), neonatal lupus erythematosus (NLE), and congenital complete heart block (CCHB). Other clinical manifestations seen in lupus patients are photosensitive rashes, interstitial pneumonitis, nephritis, and thrombocytopenia[1].

NLE is a syndrome of cutaneuous lupus, or CCHB, or both, and/or systemic manifestations which occur in children of mothers with SLE, Sjögren's syndrome or other systemic rheumatic diseases, or asymptomatic mothers with anti-Ro/SSA antibody[2,3]. CCHB is an irreversible intrauterine-acquired cardiac manifestation of NLE, caused by transplacental passage of maternal antibodies to Ro/SSA and La/SSB antigens, which

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† Presented at the annual meeting of the Royal College of Physicians of Thailand, Lotus Pang Suan Kaew Hotel, Chiang Mai, 22-25 April 1997

react with fetal myocardial tissue[2,3]. This autoantibody has also been associated with transient dermatitis, thrombocytopenia and hepatitis in NLE[2]. In Thailand, only one case of NLE with thrombocytopenia and skin rashes has been described[3]. We recently saw a patient with clinically unclassified connective tissue disease who gave birth to a child with CCHB 2 years earlier.

CASE REPORT

A 37-year-old female was referred to Chiang Mai University Hospital because of massive epistaxis. She had been healthy until one week before this admission when she developed massive epistaxis. Significant laboratory finding was a thrombocytopenia of 12,000 cells/mm^3. Thirteen units of platelet concentrate were given, but the bleeding persisted and the platelet counts remained very low, around 16,000 cells/mm^3. There was no history of alopecia, arthritis or arthralgia, photosensitivity, skin rashes, oral and genital ulcers, Raynaud's phenomenon, dry eyes or dry mouth. There was no family history of bleeding disorders. Her medical history showed that she had given birth to a full term male infant with CCHB two years earlier. The only serologic study performed on this patient at that time was antinuclear antibody, which showed homogeneous and peripheral patterns. The serologic study in the infant was not performed.

Her vital signs were normal. The only significant physical findings were mild pallor and severe epistaxis. No petichial hemorrhage or echymosis was noted.

A complete blood count showed a hemoglobin of 10.6 g/dL, hematocrit of 32 vol per cent, white blood count of 10,500 cells/mm^3 with normal differential counts and platelet counts of 26,000 cells/mm^3. Urine analysis was normal. A bone marrow study showed hypercellular marrow with increased megakaryocytes. The erythroid and myeloid series were normal. The findings were compatible with immune thrombocytopenia. Immunologic studies showed positive antinuclear antibody with speckled pattern and positive anti-Ro/SSA antibody. The antibodies to La/SSB, Sm, RNP and dsDNA were all negative. Other laboratory tests including rheumatoid factors, VDRL, Coombs' test, C3, CH50, thyroid functions, liver and renal functions were all normal or negative.

Intravenous hydrocortisone (400 mg/day) was prescribed. The platelet counts returned to normal after 8 days of therapy. Hydrocortisone was changed to oral prednisolone (50 mg/day), which was gradually tapered off and discontinued after 4 months. Recently, the patient was in good health and her blood counts were normal, and she was off all medication.

The patient's son at the final visit was 2 years old and healthy. His birth weight was 3350 g and the APGAR score at birth was 10. There were no skin rashes, jaundice or petichial hemorrhage at birth. A complete heart block with a ventricular rate of 76 beat/min was demonstrated on the electrocardiograph at birth. Current physical findings were all normal. The complete heart block persisted without symptoms. A trivial atrial septal defect was demonstrated in an echocardiograph. Serologic studies including antibodies to nuclear antigen, Sm, RNP, Ro/SSA, La/SSB, and dsDNA were all negative.

DISCUSSION

Anti Ro/SSA antibody has been found in 1-3 per cent of normal pregnant women sera[5,6], but it was found in 35-100 per cent of sera of women with children with CCHB[5-8]. The risk of the development of CCHB increases 22-fold in pregnant women who have anti-Ro/SSA antibody[6]. Waltuck et al[8] found that 23 of 57 mothers (40%) of infants with CCHB were clinically asymptomatic at the time of delivery, while the symptomatic mothers had SLE, Sjögren's syndrome and undifferentiated autoimmune syndrome (15, 8 and 11 cases respectively). Within a mean duration of follow-up of 3.7 years, 48 per cent of these asymptomatic mothers developed some rheumatic diseases in which undifferentiated connective tissue disease was the most commonly seen (26%), followed by SLE (13%) and Sjögren's syndrome (9%). Press et al[7] found that 42 of 62 mothers (66%) were healthy at the time of delivery, and 36 of these mothers remained well after a follow-up period of 12 years. Only one of the initial 42 asymptomatic mothers developed SLE with a follow-up of 10 years. McCue et al[9] found that 63 per cent of his 23 mothers of infants with CCHB showed some evidence of connective tissue disease and 7 had SLE. Only 4 of these 23 mothers had positive serology but were asymptomatic. From

these studies, approximately 40-60 per cent of mothers of infants with CCHB were asymptomatic and 28-48 per cent developed some connective tissue diseases during follow-up. Our patient developed her first clinical symptoms related to autoimmune disease (immune thrombocytopenia) 2 years after her first delivery. However, she showed no clinical symptoms suggesting systemic lupus erythematosus or Sjögren's syndrome.

The incidence of isolated CCHB has been reported as 1:20,000 live births in the U.S.A., in which 75 per cent had structural cardiac damage (10). In those without structural cardiac damage, CCHB has been found to be strongly associated with anti-Ro/SSA antibody(5-9). CCHB usually manifests late during the second and third trimester when the IgG of anti-Ro/SSA antibody passes the placenta and reacts with fetal Ro/SSA antigen which begins to develop in the myocardium and the conduction system at 10 weeks of gestation (11,12). The presence of CCHB has been reported to be associated with a high titer of anti-Ro/SSA antibody in mothers(5). Prenatal death has been reported in up to 33 per cent(13). Although intrauterine fetal heart block has been treated successfully with corticosteroids(14,15), patients with structural cardiac lesions and an early fetal heart rate of less than 55 beats/min have a poor outcome(13,16). Up to 50 per cent of the isolated CCHB cases required pacemaker implantation (8,13). The anti-Ro/SSA antibody usually is not detectable 3 months after delivery, which supports the transplacental transmission of maternal antibody(5,17). The reasons that all infants with anti-Ro/SSA antibody positive mothers do not develop cardiac abnormality, and that the cardiac system of these mothers are unaffected by this antibody are not known.

This case represents another case of an association between anti-Ro/SSA antibody and CCHB. Although the son of this patient had a trivial atrial septal defect, this does not explain the development of CCHB. Anti-Ro/SSA antibody was undetectable in her 2 year-old son; this is consistent with cases previously described in which the antibody usually disappeared after 3 months of delivery(5,17). Unfortunately, we did not have a chance to study his serology at birth. Since the majority of mothers of infants with CCHB are asymptomatic, it is important to screen all these mothers for connective tissue diseases, and the presence of antinuclear and anti-Ro/SSA antibodies should be tested.

(Received for publication on August 19, 1997)

REFERENCES

1. Harley JB, Reichlin M. Antibodies to Ro/SSA and La/SSB. In: Wallace DJ, Hahn BH, eds. Dubois' lupus erythematosus. 5th ed., Baltimore: William & Wilkins, 1997: 443-55.
2. Kitridou RC. The neonatal lupus syndrome. In: Wallace DJ, Hahn BH, eds. Dubois' lupus erythematosus. 5th ed., Baltimore: William & Wilkins, 1997: 1023-35.
3. Olson NY, Lindsley CB. Neonatal lupus syndrome. Am J Dis Child 1987; 141: 980-10.
4. Chunharas A, Tejavej A, Hathirat P, Janwityanuchit S, Jarusutus S. Neonatal lupus erythematosus in Thailand. J Med Assoc Thai 1993; 76: 218-21.
5. Taylor PV, Taylor KF, Norman A, Griffiths S, Scott JS. Prevalence of maternal Ro (SS-A) and La (SS-B) autoantibodies in relation to congenital heart block. Br J Rheumatol 1988; 27: 128-32.
6. McCredie M, Celermajer J, Sholler G, et al. A case-contol study of congenital heart block: Association with maternal antibodies to RO (SS-A) and LA (SS-B). Br J Rheumatol 1990; 29: 10-4.
7. Press J, Uziel Y, Laxer RM, Luy L, Hamilton RM, Silverman ED. Long-term outcome of mothers of children with complete congenital heart block. Am J Med 1996; 100: 328-32.
8. Waltuck J, Buyon JP. Autoantibody-associated congenital heart block: Outcome in mothers and children. Ann Intern Med 1994; 120: 544-51.
9. McCue CM, Mantakas ME, Tingelstad JB, Ruddy S. Congenital heart block in newborns of mothers with connective tissue disease. Circulation 1977; 56: 82-90.
10. Michaelsson M, Engle MA. Congenital complete

heart block: An international study of the natural history. Cardiovascular Clins 1972; 4: 86-101.
11. Deng JS, Bair LW, Shen-Schwarz S, Ramsey-Goldman R, Medsger T. 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. Groves AMM, Allan LD, Rosenthal E. Outcome of isolated congenital complete heart block diagnosed in utero. Heart 1996; 75: 190-4.
14. Chopel JA, Buyon JP, Kleinman CS. Successful in utero therapy of fetal heart block. Am J Obstet Gynecol 1995; 173: 1384-90.
15. Buyon J, Roubey R, Swersky S, et al. Complete congenital heart block: Risk of occurrence and therapeutic approach to prevention. J Rheumatol 1988; 15: 1104-8.
16. Machado MV, Tynan MJ, Curry PV, Allan LD. Fetal complete heart block. Br Heart J 1988: 60: 512-5.
17. Scott JS, Maddison PJ, Talor PV, Esscher E, Scott O, Skinner RP. Connective tissue disease, autoantibodies to ribonucleoprotein, and congenital heart block. N Engl J Med 1983; 309: 209-12.

โรคเนื้อเยื่อเกี่ยวพันในมารดาของทารกที่มีภาวะ complete heart block โดยกำเนิด: รายงานผู้ป่วย 1 ราย

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ความสัมพันธ์ระหว่าง complete heart block ที่เป็นมาแต่กำเนิดกับแอนติ Ro/SSA แอนติบอดี้เป็นที่ทราบกันดี แต่ความสัมพันธ์นี้ไม่เคยมีรายงานในประเทศไทย ผู้รายงานขอเสนอผู้ป่วยหญิงอายุ 37 ปีเข้ารับการรักษาด้วยอาการเลือดกำเดาไหลไม่หยุดจากเกร็ดเลือดต่ำ ผู้ป่วยให้กำเนิดเด็กชายที่มีภาวะ complete heart block เมื่อ 2 ปีแล้วซึ่งในขณะนั้นผู้ป่วยมีสุขภาพสมบูรณ์ การตรวจเลือดพบแอนตินิวเคลียร์แอนติบอดี้และแอนติ Ro/SSA แอนติบอดี้ในมารดา แต่ไม่พบแอนติบอดี้ดังกล่าวในบุตร ผู้รายงานได้รายงานความสัมพันธ์ระหว่างแอนติ Ro/SSA แอนติบอดี้และผลลัพธ์ในมารดาและเด็กทารก

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