CASE REPORT

A Case of Neonatal Lupus Erythematosus Showing Transient Anemia and Hepatitis

Kyu Ri Kim, M.D., Tae Young Yoon, M.D.

Department of Dermatology, School of Medicine and Medical Research Institute, Chungbuk National University, Cheongju, Korea

Neonatal lupus erythematosus (NLE) is an autoimmune disease that is associated with transplacental passage of maternal autoantibodies that are reactive to SSA/Ro and SSB/La antigens. Cardiac involvement, hematologic abnormality and hepatic disease may occur in the infants suffering with NLE, in addition to the characteristic skin lesions. We report here on a case of NLE in a 4-week-old female infant who was born to an asymptomatic mother, and the baby displayed the characteristic clinical and histological features of cutaneous NLE with transient anemia and hepatitis. Both the infant and mother were positive for anti-SSA/Ro and anti-SSB/La. There have been 18 case reports of NLE in the Korean literature, including 7 case reports in the dermatological field. We describe herein another case of NLE that showed transient anemia and hepatitis, and we also review the case reports of NLE in the Korean literature. (*Ann Dermatol* 21(3) 315 ~ 318, 2009)

-Keywords-

Anemia, Anti-SSA/Ro, Anti-SSB/La, Hepatitis, Neonatal lupus erythematosus

INTRODUCTION

Neonatal lupus erythematosus (NLE) is an uncommon immune-mediated disease that is associated with transplacental transfer of maternal IgG autoantibodies. Approximately half of the affected neonates have congenital

heart block (CHB). Cutaneous lesions occur in approximately 50% of these patients and they typically consist of transient, erythematous, annular, and scaling plaques in sun-exposed areas, and these lesions resemble subacute cutaneous lupus erythematosus both clinically and histologically. Skin lesions and heart block are seen simultaneously in less than 10% of the patients with NLE¹. Transient hepatitis, anemia, and thrombocytopenia can also occur²⁻¹⁰.

There have been 18 case reports of NLE in the Korean literature, including 7 case reports in the dermatological field of which 3 cases showed anemia and hepatitis (Table 1)⁶⁻²². We describe herein another case of NLE that displayed transient anemia and hepatitis. In addition, we review the cases of NLE in the Korean literature.

CASE REPORT

A 4-week-old, full-term, female infant, whose birth and life had been otherwise gone well, was brought to the dermatological clinic with a 3-week history of erythematous and annular plaques on the face and lower extremities (Fig. 1). The physical examination revealed no other abnormalities.

A biopsy from the face showed slight keratin plugging of the hair follicles, focal hydropic degeneration of the basal layer in the epidermis and a patchy perivascular, periadnexal, and interstitial infiltrate of lymphohistiocytes in the whole dermis (Fig. 2).

The patient's antinuclear antibody (ANA) titer was 1 : 320 with a homogeneous pattern. The tests for anti-SSA/Ro antibody and anti-SSB/La antibody were positive. The results of the electrocardiogram (ECG) were normal, but mild anemia (hemoglobin 8.3 g/dl) and hepatitis (AST/ALT 75/112 IU/L) were present.

The 25-year-old mother had no history of connective tissue disease and she was asymptomatic. The serological

Received November 11, 2008, Accepted for publication March 1, 2009
*This work was supported by the research grant of the Chungbuk National University in 2008.

Reprint request to: Tae Young Yoon, M.D., Department of Dermatology, School of Medicine & Medical Research Institute, Chungbuk National University, 410, Seongbong-ro, Heungdeok-gu, Cheongju 361-763, Korea. Tel: 82-43-269-6369, Fax: 82-43-266-1698, E-mail: tyyoon@chungbuk.ac.kr

Table 1. The clinical and serologic features of the reported cases of neonatal lupus erythematosus in the Korean literature

	Sex/ Day-old	Skin lesion	Site	ANA profile					ECG	CBC/ LFT
				Titer	Anti- dsDNA	Anti- Ro	Anti- La	Anti- U ₁ RNP		
Chu et al. ⁶	M/1	AE	Face	+	+	+	+	—	CHB	PLT 69,000 AST/ALT 336/591
Shin et al. ⁷	M/40	AE	Face, Ext	+	+	+	+	+	Normal	Hb 7.5 AST/ALT 131/871
Park et al. ⁸	M/1	AE	Face	+	+	+	+	—	Normal	Hb 13.8 PLT 37,000
Chung and Chey ⁹	F/30	AE	Face, Ext	+	NP	+	+	NP	Normal	Hb 9 AST/ALT 137/150
Lee et al. ¹⁰	M/40	Papule	Whole body	+	+	+	+	—	Normal	Hb 7.2 AST/ALT 110/73
Kim et al. ¹¹	M/30	AE	Face	1 : 40	+	+	—	—	CHB	Normal
Lee et al. ¹²	F/84	AE	Face	1 : 160	NP	—	+	NP	Normal	Normal
Choi et al. ¹³	M/60	ND	ND	+	+	+	—	—	Normal	Normal
Kim et al. ¹⁴	F/1	ND	ND	+	—	+	+	—	CHB	Normal
Chung et al. ¹⁵	M/1	ND	ND	+	—	+	+	—	CHB	Normal
Kwon et al. ¹⁶	F/25	AE	Whole body	+	—	+	+	NP	Normal	Normal
	M/30	AE	Face, Ext	+	—	+	+	NP	Normal	Normal
Oh and Lee ¹⁷	M/50	AE	Face, Trunk	1 : 2,560	—	—	—	+	Normal	Hb 9.2
Noh et al. ¹⁸	M/28	Target-like	Face, Ext	1 : 320	—	+	+	NP	Normal	Normal
Jung et al. ¹⁹	M/1	ND	ND	+	+	+	+	—	CHB	Normal
Ahn et al. ²⁰	F/28	AE	Whole body	1 : 80	—	—	—	+	Normal	Normal
Hong et al. ²¹	M/10	Target-like	Whole body	1 : 80	+	+	+	—	Normal	Normal
Park et al. ²²	M/29	AE	Face, Ext	1 : 160	—	—	+	NP	Normal	Normal
Present case	F/30	AE	Face, Ext	1 : 320	—	+	+	NP	Normal	Hb 8.3 AST/ALT 75/112

AE: annular erythema, ALT: alanine aminotransferase, ANA: antinuclear antibody, AST: aspartate aminotransferase, CBC: complete blood count, CHB: congenital heart block, ECG: electrocardiogram, Ext: extremity, Hb: hemoglobin, LFT: liver function test, ND: not described, NP: not performed, PLT: platelet

Fig. 1. Erythematous and annular plaques on the face.

studies of the mother showed the presence of anti-SSA/Ro antibody and anti-SSB/La antibody. The mother's ANA titer was 1 : 640 with a homogeneous pattern.

The patient received topical corticosteroid and the skin lesions completely disappeared 6 months later without any residual atrophy or hyperpigmentation. At that time, the infant had an ANA titer less than 1 : 40; both anti-SSA/Ro antibody and anti-SSB/La antibody became negative and the complete blood cell count and liver function tests were normal.

DISCUSSION

NLE is an uncommon autoimmune disease that is associated with the transplacental transfer of maternal IgG

Fig. 2. Slight keratin plugging of the hair follicles, focal hydropic degeneration of the basal layer in the epidermis and a patchy perivascular, periadnexal, and interstitial infiltrate of lymphohistiocytes in the whole dermis (H&E, $\times 100$).

autoantibodies. Only 1% of neonates develop NLE if the mother has autoantibodies. If an anti-SSA/Ro positive mother has one child with NLE, then 25% of the future siblings will also be affected. In 95% of the cases, the autoantibody is anti-SSA/Ro, but it can be anti-SSB/La or anti-U₁RNP¹. Any of these autoantibodies can be found alone or in combinations. Only cutaneous disease has been reported for the cases where only anti-U₁RNP antibodies are found^{20,23}. There are even reports of histological documented cases of NLE where none of the above-listed antibodies were found²⁴. This finding suggests that antibodies other than anti-SSA/Ro, anti-SSB/La, or anti-U₁RNP can be involved in some cases, and perhaps by some factor or cofactor that has yet to be determined.

The major clinical manifestations of NLE are cardiac problems, including CHB, and cutaneous lesions¹. CHB can result in congestive heart failure and the subsequent placement of a pacemaker. In one investigation, 57% of these patients eventually required a pacemaker²⁵. CHB is associated with a 20~30% mortality rate during the neonatal period. Deaths may also occur later in life as a result of the failure of the pacemaker. There have been five CHB patients reported in the Korean literature. Among them, three showed a spontaneous remission, one needed pacemaker insertion and one passed away. On the other hand, the cutaneous lesions of NLE consist of transient non-scarring erythematous annular plaques with a predilection for the periorbital and photodistributed areas. These lesions generally appear within the first 2 months of life and they resolve within 4 to 6 months when the maternal antibodies disappear. In rare cases, remnant telangiectasias can occur at the previously affected sites²⁶.

Hepatic and hematologic abnormalities are observed in approximately 10% of the infants with NLE¹⁰. Hepatitis, hyperbilirubinemia, liver failure, thrombocytopenia, and anemia can occur²⁻¹⁰. The prognosis of a NLE patient with liver failure is poor, whereas for the NLE patients with other manifestations, the prognosis is good with transient involvement and spontaneous resolution. In the Korean literature, anemia occurred in 5 cases, thrombocytopenia occurred in 2 cases, and hepatitis occurred in 4 cases. Only 3 cases showed anemia and hepatitis simultaneously. Our patient showed typical cutaneous lesions, transient hepatitis, and anemia without cardiac involvement.

The association of NLE with maternal autoantibodies is a strong indicator of the importance of autoantibodies for determining the pathogenesis of NLE²⁷. In patients with NLE, the autoantibodies are maternal in origin and they disappear by 6 months of age. These autoantibodies have the capacity to cause direct injury to the skin and the cardiac, hepatobiliary and hematologic system²⁸. The disappearance of autoantibodies parallels the disappearance of the cutaneous, hematologic, and hepatic abnormalities. However, in patients suffering with CHB, immunodeposits of autoantibodies may result in fibrosis and calcification in and around the atrioventricular node, which can lead to permanent conduction defects.

The diagnosis of NLE is generally based on the clinical findings when there are maternal and/or neonatal autoantibodies present. Determining the titers of ANA and anti-SSA/Ro, anti-SSB/La, and anti-U₁RNP antibodies is recommended for making the diagnosis. Liver function tests and a complete blood cell count should also be done. All the patients suspected of having NLE should undergo a thorough cardiac examination.

Spontaneous resolution is the natural course of the cutaneous lesions. However, management of the skin lesions of NLE requires avoiding sun light and using sunscreen and low-potency topical corticosteroids to hasten resolution. Treatment of the heart block is not necessary unless cardiac failure is evident.

Many (40%) of the affected infants' mothers are asymptomatic. They might have Sjögren's syndrome, systemic lupus erythematosus, rheumatoid arthritis, overlap syndrome or even leukocytoclastic vasculitis. Although the outlook of these mothers appears to be generally good, there is the possibility of developing serious autoimmune disease²⁹. Thus, close observation is necessary for the mothers of infants with NLE.

In conclusion, we describe here an additional case of NLE that displayed transient anemia and hepatitis.

REFERENCES

1. Lee LA. Neonatal lupus erythematosus. *J Invest Dermatol* 1993;100:9S-13S.
2. Esterly NB. Neonatal lupus erythematosus. *Pediatr Dermatol* 1986;3:417-424.
3. Dickerson PA, Prendiville JS. Thrombocytopenia and hepatosplenomegaly in a newborn. *Pediatr Dermatol* 1989;6:346-348.
4. Watson R, Kang JE, May M, Hudak M, Kickler T, Provost TT. Thrombocytopenia in the neonatal lupus syndrome. *Arch Dermatol* 1988;124:560-563.
5. Wolach B, Choc L, Pomeranz A, Ben Ari Y, Douer D, Metzker A. Aplastic anemia in neonatal lupus erythematosus. *Am J Dis Child* 1993;147:941-944.
6. Chu TG, Back YW, Huh JW, Lee CY, Chung HK, Park JS. A case of neonatal lupus syndrome with congenital heart block. *J Korean Soc Neonatol* 1997;4:260-266.
7. Shin DY, Seok SM, Koo DW. Neonatal lupus erythematosus. *Korean J Dermatol* 1999;37:1649-1654.
8. Park SH, Kim HJ, Yoo KH, Hong YS, Lee JW, Kim SK. A case of neonatal lupus erythematosus with pancytopenia and bradycardia. *J Korean Soc Neonatol* 2001;8:150-155.
9. Chung JY, Chey MJ. A case of neonatal lupus with abnormal liver function test and skin lesion. *Korean J Pediatr* 2005;48:85-87.
10. Lee SM, Ham SS, Jeon IS, Son DW. Neonatal lupus erythematosus manifests as pancytopenia and mildly abnormal liver functions. *Korean J Perinatol* 2005;16:317-321.
11. Kim CR, Chang YP, Kim HS, Kim MJ, Kim BI, Choi JH, et al. Outcome in infants of mothers with systemic lupus erythematosus. *J Korean Pediatr Soc* 1993;36:791-804.
12. Lee HP, Lee HN, Houh D, Byun DG, Baek SC. Neonatal lupus erythematosus. *Ann Dermatol* 1998;10:185-189.
13. Choi JW, Kim MH, Kim ST, Park HJ. A case of neonatal lupus syndrome with acute myocarditis. *J Korean Pediatr Soc* 1999;42:1298-1303.
14. Kim GS, Choi SM, Lee GH. Two cases of neonatal arrhythmia observed by fetal echocardiography. *Korean J Perinatol* 1999;10:71-79.
15. Chung SH, Lee Y, Cheon YH, Jung IC, Yoon WS, Lee JS, et al. A case of neonatal lupus syndrome with congenital complete heart block. *Korean J Obstet Gynecol* 2002;45:723-727.
16. Kwon IH, Yoo JY, Lee JH, Cho KH. Two cases of neonatal lupus erythematosus. *Korean J Dermatol* 2003;41:956-959.
17. Oh DH, Lee CW. Neonatal lupus erythematosus. *Korean J Dermatol* 2003;41:1108-1110.
18. Noh Y, Lee GC, Eo SH, Ha TS, Kim MK, Kim CY, et al. Neonatal lupus erythematosus: showing target-like skin lesions. *Korean J Dermatol* 2003;41:1228-1231.
19. Jung KS, Shin SH, Choi CW, Lee JH, Kim SI. A case of complete atrioventricular block in neonatal lupus erythematosus. *Korean J Med* 2004;67:s887-s891.
20. Ahn BH, Lee GC, Yoon TY, Kim MJ. A case of neonatal lupus erythematosus associated with anti-U1RNP antibodies. *Korean J Pediatr* 2005;48:342-345.
21. Hong SJ, Hwang IJ, Kim DH. Neonatal lupus syndrome. *J Korean Rheum Assoc* 2005;12:245-246.
22. Park G, Jang HC, Chung H. A case of neonatal lupus erythematosus. *Korean J Dermatol* 2006;44:124-126.
23. Dugan EM, Tunnessen WW, Honig PJ, Watson RM. U1RNP antibody-positive neonatal lupus. A report of two cases with immunogenetic studies. *Arch Dermatol* 1992;128:1490-1494.
24. Crowley E, Frieden IJ. Neonatal lupus erythematosus: an unusual congenital presentation with cutaneous atrophy, erosions, alopecia, and pancytopenia. *Pediatr Dermatol* 1998;15:38-42.
25. Neonatal lupus erythematosus. In: Hurwitz S, editor. *Clinical pediatric dermatology: a textbook of skin disorders of childhood and adolescence*. 2nd ed. Philadelphia: W B Saunders, 1993:567-569.
26. Thornton CM, Eichenfield LF, Shinall EA, Siegfried E, Rabinowitz LG, Esterly NB, et al. Cutaneous telangiectases in neonatal lupus erythematosus. *J Am Acad Dermatol* 1995;33:19-25.
27. Lee LA. Transient autoimmunity related to maternal autoantibodies: neonatal lupus. *Autoimmun Rev* 2005;4:207-213.
28. Sontheimer RD, McCauliffe DP. Pathogenesis of anti-Ro/SS-A autoantibody-associated cutaneous lupus erythematosus. *Dermatol Clin* 1990;8:751-758.
29. McCune AB, Weston WL, Lee LA. Maternal and fetal outcome in neonatal lupus erythematosus. *Ann Intern Med* 1987;106:518-523.