Neonatal Lupus Erythematosus: A 20-Year Retrospective Study

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Objective: *To study clinical manifestations, investigations, treatment and outcomes of neonatal lupus erythematosus (NLE) patients and their mothers.*

Material and Method: *A retrospective descriptive study was performed to review the neonatal lupus erythematosus patients and their mothers at Queen Sirikit National Institute of Child Health during January 1993 to December 2013. The diagnostic criteria required the presence of clinical symptoms plus positive anti-Ro/SSA or anti-La/SSB or both.*

Results: *There were 34 cases, 12 males and 22 females. Age of onset of clinical manifestations was from birth to 60 days with median age of 21 days. Cutaneous, hepatobiliary, hematological and cardiac abnormalities were found in 88.2%, 61.2%, 50%, 14.7%, respectively. Cutaneous lesions included erythematous rash (70%), annular lesions (75.8%), petechiae (26.6%), raccoon eyes (26.6%), and telangiectasia (20%). Among those with hepatic involvement (n = 18), transaminitis was the most common finding (100%) followed by hepatosplenomegaly (38.8%) and cholestasis (22.2%). Seventeen cases (50%) had hematological problems including anemia (29.4%) and anemia with thrombocytopenia (20.6%). The most severe complication, complete heart block was found in 14.7% (n = 5). Anti-Ro/SSA and anti-La/SSB were positive in 91.1% and 58.8% of cases, respectively. All four babies with complete heart block were treated with pacemaker. Systemic corticosteroids were given to eleven babies due to severe skin lesions and hepatic involvement. There was no mortality during the study. Most neonatal lupus erythematosus mothers (24 cases, 74.2%) were asymptomatic. Ten mothers (25.8%) were diagnosed as autoimmune diseases (systemic lupus erythematosus in 6 cases and other autoimmune diseases in 4 cases). However, 7 of 24 asymptomatic mothers developed SLE within 3 years after delivery.*

Conclusion: *NLE should be suspected among neonates or young infants presenting with congenital heart block or skin rash with multi-system involvement despite a lack of concurrent maternal autoimmune diseases. Anti-Ro/SSA and/or anti-La/SSB are the most useful laboratory diagnosis. Most NLE patients without congenital heart block have relatively good prognosis.*

Keywords: *Neonatal lupus erythematosus, Cutaneous, Hepatobiliary, Hematological, Congenital heart block*

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Neonatal lupus erythematosus (NLE) is an uncommon autoimmune disease associated with maternal antiRo/SSA, antiLa/SSB and less commonly, U1-ribonucleoprotein (U1-RNP) antibodies[1-5]. The disease was first described in 1954 by McCuistion and Schoch who reported a case of transient lupus skin lesions in an infant with an ANA-positive mother[6]. NLE affects multiple systems such as dermatologic, hematologic, hepatobiliary and cardiac system. Most of the mothers of NLE patients are asymptomatic when the infants are diagnosed with the disease but they may have clinical signs of systemic lupus erythematosus (SLE) or other autoimmune disorders later. The clinical course of NLE is usually benign and self-limited but sometimes it may be associated with serious sequelae especially congenital heart block[1-5].

Several studies of neonatal lupus erythematosus have been reported worldwide[7-12]. However, there have been few series case reports[9-12]. The authors reviewed all the NLE cases over a 20 years period at Queen Sirikit National Institute of Child Health, which is the tertiary care children's hospital in Bangkok, Thailand.

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Material and Method

A retrospective study was performed to review the neonatal lupus erythematosus patients and their mothers at Queen Sirikit National Institute of Child Health during January 1993 to December 2013. The

criteria for diagnosis of NLE were clinical characteristic with positive antiRo/SSA or antiLa/SSB or both. We reviewed clinical manifestations, immunological, treatment and outcome of the patients along with the mothers health status and immunological profiles.

Results

Thirty-four cases (12 males, 22 females) were identified during the 20 years study period. Male to female ratio was 1 to 1.8. The age of onset was from at birth to 60 days. Thirty-two cases (94%) had the symptoms within 1 month of age. Mean birth weight was 2,542±404 grams.

Cutaneous, hepatobiliary, hematological, and cardiac abnormalities were found in 88.2%, 52.9%, 50%, 14.7%, respectively. Twenty-four cases (71%) had multiple organs involvement. Ten cases (29%) had only one affected organ (Table 1).

Clinical data, laboratory findings, treatment, and course of the disease in these patients and their mothers are summarized in Table 2.

The cutaneous findings were the most common abnormalities found in 30 cases (88.2%) including erythematous rash (70%), annular lesions (36.6%) (Fig. 1), petechiae (26.6%), raccoon eyes (26.6%) (Fig. 2), and telangiectasia (20%) (Table 3). The face and scalp were the most common location seen in 29 cases (99.6%).The extremity and trunk were found in 53.3% and 43.3%, respectively. Twenty-eight cases were treated with topical corticosteroids with good response. Short course of oral prednisolone was given in 2 cases (case 18 and 25) due to widespread skin lesions. Most cutaneous lesions completely resolved. Residual skin changes were petechiae (6 cases), hypopigmentation (4 cases), hyperpigmentation (3 cases), atrophy (2 cases) and telangiectasia (1 case). Cutaneous rash was an isolate finding in only 6 cases (No. 6, 11, 18, 19, 20, 21). The others had skin and multiple organ involvements.

Hepatobiliary changes were the second most common manifestations and were seen in 18 cases (52.9%). All of the patients had asymptomatic elevated liver enzyme while eight had hepatosplenomegaly and four had cholestasis jaundice. Nine cases with severe hepatitis were treated with oral prednisolone for 4-8 weeks while the rest received supportive treatment.

Hematological changes were observed in 17 cases (50%) including anemia in 10 cases (29.4%), anemia with thrombocytopenia in 7 cases (20.6%). Four cases (No. 5, 8, 30, 34) with severe anemia and thrombocytopenia were treated with blood component transfusion.

Cardiac involvement was found at birth in 5 cases (14.7%). Complete heart block and second degree arterioventricular block were found in 4 cases and 1 case, respectively. Interestingly, three cases (No. 1, 2, 3) with complete heart block, who had isolate cardiac problems, were born to SLE mothers. Another case (No. 4) with second degree AV block that had cutaneous and hepatic involvement was also born to SLE mother. Only 1 case (No. 17) with complete heart block and patent ductus arteriosus was born to an asymptomatic mother. Pacemakers were performed in 4 cases due to complete heart block.

The immunological profile of the NLE patients showed that 31 cases (91.1%) had positive antiRo/SSA, twenty cases (58.8%) positive antiLa/SSB and eighteen cases (52.9%) positive for both antiRo/SSA and antiLa/SSB. The maternal sera were positive for antiRo/SSA in 24 cases (92.3%) and antiLa/SSB in18 cases (69.2%) (Table 4).

Most of NLE mothers (24 cases, 74.2%) were asymptomatic at the time when their babies were diagnosed with NLE. Ten mothers (25.8%) were diagnosed with autoimmune diseases (systemic lupus erythematosus 7 cases, hyperthyroidism 2 cases and polyarteritis nodosa 1 case). However, 7 of 24 asymptomatic mothers developed SLE 1 month to 3 years later (No. 11-16).Two mothers died due to severe SLE during the follow-up period, one during immediate

Table 1. Clinical manifestations of NLE patients (n = 34)

Clinical manifestations	No.	%
Skin rash only	6	17.6
Congenital heart block only	4	11.9
Skin rash + congenital heart block + hepatobiliary changes	1	2.9
Skin + hematological changes	7	17.6
Skin + hepatobiliary changes	6	20.6
Skin + hepatobiliary changes + hematological changes	10	29.4

Table. 2 Clinical data, immunological profiles, treatment and outcome of the NLE babies and mothers

Case	Sex	Maternal disease		Birth weight (g)	Onset (days)	Systemic involvement	Patient serology			Maternal serology			Treatment	Follow-up (mo)
		At delivery	Follow-up				Anti-Ro	Anti-La	ANA	Anti-Ro	Anti-La	ANA		
1.	M	SLE	SLE	2,500	At birth	Complete AV block	+	-	1:256	NA	NA	NA	Pacemaker	38
2.	M	SLE	SLE	2,835	At birth	Complete AV block	+	-	NA	+	-	1:1,280	Pacemaker	18
3.	F	SLE	SLE	2,200	At birth	Complete AV block	+	-	NA	NA	NA	NA	Pacemaker	5
4.	M	Hyperthy roidism	SLE, 4 mo	2,790	20	2nd degree AV block, skin rash, elevated transaminases, hepatosplenomegaly	+	+	1:320	+	+	1:160	Supportive, topical steroid	38
5.	F	SLE	Dead	1,465	At birth	Skin rash, elevated transaminaseschol estasis jaundice, anemia, thrombo cytopenia	+	-	-	+	-	1:80	Topical steroid, ursofalk, PRC	104
6.	F	SLE	SLE	2,900	30	Skin rash	+	-	1:80	+	+	1:1,280	Topical steroid	90
7.	F	SLE	SLE	2,300	14	Skin rash, elevated transaminases, anemia	+	+	1/320	NA	NA	NA	Topical steroid	3
8.	F	SLE	SLE	2,380	7	Skin rash, elevated transaminases, anemia	+	+	NA	+	+	NA	Topical steroid, PRC	3
9.	F	PAN	PAN	2,450	10	Skin rash, anemia	+	+	NA	-	+	NA	Supportive	12
10.	F	Hyperthy roidism	SLE, 15 mo	2,400	7	Skin rash, elevated transaminases	+	+	NA	+	+	NA	Systemic & topical steroid	26
11.	F	No	SLE, 1 mo	2,800	At birth	Skin rash	+	-	1:1,280	+	-	1:1,280	Topical steroid	48
12.	F	No	Dead, 7 mo	2,370	At birth	Skin rash, elevated transaminases, Hepatosplenomegaly, anemia, thrombocytopenia	+	-	NA	NA	NA	NA	Supportive	25
13.	M	No	SLE, 3 mo	2,330	At birth	Skin rash, elevated transaminases, hepatomegaly, anemia, thrombocytopenia	+	-	NA	+	+	NA	Topical steroid	9
14.	F	No	SLE, 36 mo	1,860	30	Skin rash, elevated transaminases	+	+	NA	+	+	NA	Topical steroid	4
15.	M	No	SLE, 1 mo	2,780	14	Skin rash, elevated transaminases, anemia	+	+	1:1,280	+	+	1:5,120	Systemic & topical steroid	33
16.	F	No	SLE, 2 mo	2,560	30	Skin rash, elevated transaminases, cholestasis jaundice, hepatosplenomegaly, anemia, thrombocytopenia	+	+	NA	+	+	1:5,120	Systemic & topical steroid, ursofalk	18

ANA = antinuclear antibody; NA = not available; AV = arterioventricular; SLE = systemic lupus erythematosus; PAN = polyarteritis nodusa

Table. 2 Cont.

Case	Sex	Maternal disease		Birth weight (g)	Onset (days)	Systemic involvement	Patient serology			Maternal serology			Treatment	Follow-up (mo)
		At delivery	Follow-up				Anti-Ro	Anti-La	ANA	Anti-Ro	Anti-La	ANA		
17.	F	No	No	3,200	At birth	Complete AV block, PDA	+	-	NA	+	-	NA	Pacemaker, PDA ligation	32
18.	M	No	No	2,990	10	Skin rash	+	-	1:256	NA	NA	+	Systemic& topical steroid	68
19.	F	No	No	2,500	14	Skin rash	+	-	-	NA	NA	NA	Topical steroid	4
20.	F	No	No	3,500	7	Skin rash	+	+	1:1,280	+	+	1:1,280	Topical steroid	48
21.	F	No	No	Unknown	30	Skin rash	-	+	NA	NA	NA	NA	Topical steroid	13
22.	M	No	No	3,100	14	Skin rash, anemia	+	+	1:1,280	+	+	1:1,280	Topical steroid	2
23.	M	No	No	2,500	45	Skin rash, anemia	+	+	1:320	+	+	1:5,120	Topical steroid	4
24.	F	No	No	2,600	30	Skin rash, anemia	+	-	1:80	+	-	1:320	Topical steroid	3
25.	F	No	No	3,294	30	Skin rash, anemia	+	+	1:80	+	+	1:320	Systemic& topical steroid	19
26.	F	No	No	2,910	30	Skin rash, anemia	+	+	NA	+	+	NA	Topical steroid	4
27.	F	No	No	2,600	3	Skin rash, elevated transaminases	+	+	1:1,280	+	+	1:1,280	Topical steroid	11
28.	M	No	No	2,990	15	Skin rash, elevated transaminases	+	-	NA	-	-	-	Systemic & topical steroid	3
29.	M	No	No	2,800	30	Skin rash, elevated transaminases, cholestasis jaundice	+	+	1:1,280	+	+	1:1,280	Systemic & topical steroid, ursofalk	27
30.	F	No	No	2,910	7	Skin rash, elevated transaminases, hepatosplenomegaly, anemia, thrombocytopenia	+	-	1:80	+	-	1:1,280	Systemic & topical steroid, PRC	56
31.	F	No	No	1,700	60	Skin rash, elevated transaminases, hepatosplenomegaly	-	-	1:1,280	+	-	1:1,280	Topical steroid	26
32.	M	No	No	3,120	15	Skin rash, elevated transaminases, anemia	+	+	1:1,280	NA	NA	NA	Systemic & topical steroid	9
33.	F	No	No	2,220	30	Skin rash, elevated transaminases, hepatosplenomegaly, anemia, thrombocytopenia	+	+	1:1,280	+	+	NA	Systemic & topical steroid	21
34.	M	No	No	2,110	At birth	Skin rash, elevated transaminases, cholestasis jaundice, hepatosplenomegaly, anemia, thrombocytopenia	+	+	NA	+	+	1:1,280	Systemic & topical steroid, ursofalk, PRC, Platelet	32

ANA = antinuclear antibody; NA = not available; AV = arterioventricular; SLE = systemic lupus erythematosus; PAN = polyarteritis nodusa

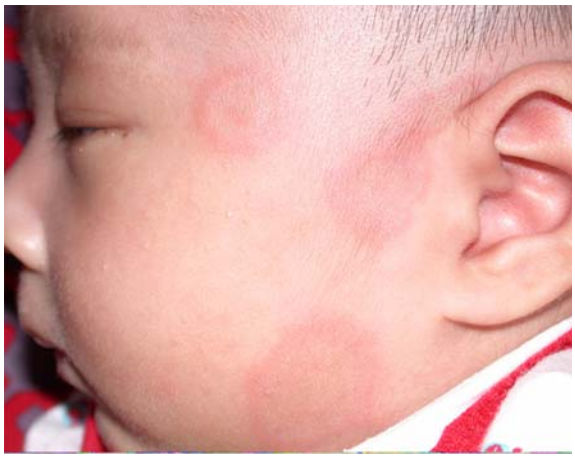

Fig. 1 Multiple annular patches on the face.

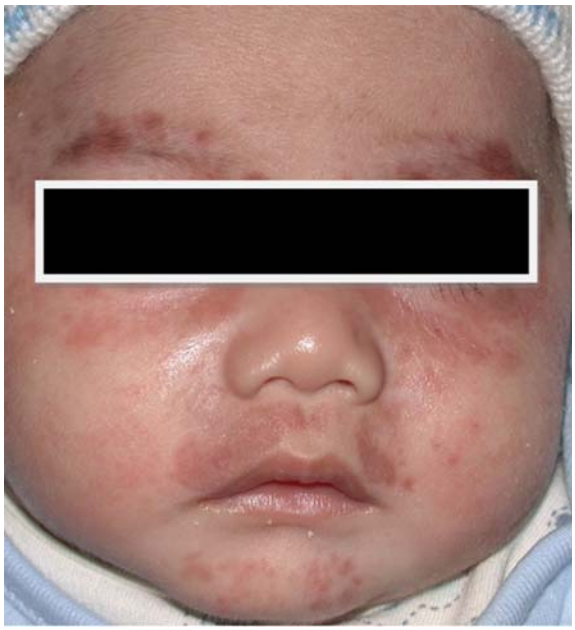

Fig. 2 Periorbital or owl eye is characteristic finding in NLE.

postpartum and another at 7 months after delivery.

The clinical manifestations resolved in most of patients. The follow-up period ranged from 2 months to 9 years. There was no mortality during this period and no patient developed any autoimmune disease.

Discussion

The present study showed that NLE is an uncommon disease. During a 20 years study period, only 34 cases were diagnosed. The true incidence of NLE is unknown, it may vary from 1 in 12,500 to 20,000 live birth due to under diagnosis[13].

Table 3. Cutaneous findings in 30 patients of NLE

Cutaneous lesions	Number of patient	(%)
Erythematous patch	21	70.0
Annular rash	11	36.6
Petechiae	8	26.6
Racoon eye	8	26.6
Telangiectasia	6	20.0

NLE is caused by maternal anti Ro/SSA or antiLa/SSB autoantibodies that pass through the placenta into the fetal circulation. The antibodies associated with heart block and cutaneous manifestations are believed to be different; antibodies against the 52/60-kD Ro/SSA and 48-kD La/SSB ribonucleoproteins are associated with heart block, whereas antibodies against the 50-kD La/SSB ribonucleoprotein are associated with the cutaneous manifestations[14,15]. Anti-U1RNP auto-antibodies are usually associated with cutaneous lesions without cardiac or systemic abnormalities[16].

Clinically, the cutaneous and cardiac are common manifestations followed by the less common hepatic and hematological manifestations. Neurological abnormalities such as asymptomatic hydrocephalus may also be affected[17,18].

Cutaneous findings of NLE patients are similar to subacute cutaneous lupus erythematosus in adult. The typical findings are round, annular patches, raccoon eyes or periorbital owl eyes[19-21]. Face and scalp are the common location but lesions can occur anywhere. The cutaneous findings usually develop during the first week of life and resolve within 6 months as maternal autoantibodies are cleared from the infant's circulation.

Differential diagnosis of skin lesions in NLE include seborrheic dermatitis, fungal infection, and/or annular erythema at infancy. The authors found that erythematous rash was the most common cutaneous finding. Annular rash and raccoon eyes were found in 36.6% and 26.6%, respectively. Isolated skin rash was found in 5 cases. Low potency topical corticosteroids and sun protection are the mainstay of therapy for cutaneous NLE. Most cases (80%) responded to topical corticosteroids treatment and 4 cases were treated with systemic corticosteroids due to severe skin lesions and hepatic involvement. All skin lesions completely resolved within 6 months. Therefore, in cases of patients with cutaneous lesions suspected of NLE, physicians

Table 4. Immunological profile in NLE patients and their mothers

Immune profile	Patients		Mothers	
	No. positive/No. done	%	No. positive/No. done	%
ANA	17/20	85	19/20	95
Anti-dsDNA	7/19	36.8	1/15	6.7
Anti-Sm	0/17	0	0/13	0
Anti-RNP	2/17	11.7	1/11	9
AntiRo/SSA	31/34	91.1	24/26	92.3
AntiLa/SSB	20/34	58.8	18/26	69.2
AntiRo/SSA & antiLa/SSB	18/34	52.9	17/26	65.4

Table 5. Comparison of NLE patients between the present and other studies

	Current Study	Wisuthsarewong et al[9]	Kobayashi et al[10]	Yang CY et al[11]	McCune et al[12]
No. of patients	34	17	193	25	24
Ethinicity	Thai	Thai	Japanese	Taiwanese	Caucasian
Maternal autoimmune disease (%)	25.8	35.3	17.1	46	47.6
Clinical manifestations (%)					
Skin rash	88.2	70.6	78	84	42
Skin rash + congenital heart block	2.9	NA	8	0	8
Congenital heart block only	14.7	52.9	15	16	50
Hepatic dysfunction	52.9	52.9	24	8	8
Hematological abnormality	50	35.3	15	8	8
Anti-Ro positive (%)	91.1	87.5	81	96	100
Require pacemaker (%)	11.7	41.2	NA	12	23.8
Dead (%)	0	11.7	NA	4	14.2

NA = not available

should look for hematological, hepatic and most importantly, cardiac abnormalities.

NLE has significant hepatobiliary involvement, which may be under diagnosed or misdiagnosed as physiologic jaundice. The hepatobiliary involvement has been reported from 10% to 53%. It can manifest as mild aminotransferase elevation, cholestatic jaundice to fulminant hepatic failure[10,22,23]. The authors found hepatobiliary manifestations in 52.9% which was higher than other previous reports[22,23]. This may be due to liver function tests being performed in all cases diagnosed as NLE. Clinicians should be aware of the wide range of hepatobiliary manifestations in NLE.

Hematological involvement in NLE includes hemolytic anemia, thrombocytopenia and/or leucopenia. It usually occurs in the first two weeks of life and generally does not require treatment[24]. The present study found anemia and thrombocytopenia in half of cases. Four cases developed severe anemia with thrombocytopenia and needed blood component transfusion.

Congenital heart block is a permanent and serious complication and mostly occurs in 15 to 30%[25-28]. The mechanism of heart block is from transplacentally maternal autoantibody binding to the antigens on the surface of myocytes of the fetus in utero that triggers the inflammatory response, causing irreversible fibrotic replacement of the conducting system of atrioventricular node and dilated cardiomyopathy. The authors found cardiac involvement in 14.7% similar to Taiwanese and Japanese study but lower than the previous report by Wisuthesereewong from Thailand and a Caucasian study, which was higher than 50%[8,9]. A pacemaker should be inserted for the neonates to prevent morbidity and mortality. The mortality rate of cardiac neonatal lupus was approximately 20%[26,27].

The overall comparison of the clinical manifestations of NLE and maternal status of the presented and other previous studies were shown in Table 5. The authors found that cutaneous and cardiac changes were similar to other studies but hepatobiliary and hematological changes were higher than other studies. Outcome of this study was good without mortality.

From the previous studies, mothers of NLE patients are initially asymptomatic in 50-70%. The presented showed that at the time of diagnosis of NLE, twenty-four cases (74%) were asymptomatic and 10 cases (26%) had SLE and other autoimmune diseases. However, during follow-up, seven cases of asymptomatic mothers developed SLE within 1 month to 3 years later. Long-term follow-up is very important for all asymptomatic mothers to look for signs and symptoms of autoimmune diseases[29]. In mothers with anti-Ro/SSA and/or anti-La/SSB antibodies and infants with congenital heart block, the risk of recurrence in subsequent offspring is 17-25%. Therefore, careful monitoring of subsequent pregnancies with serial ultrasonography and fetal echocardiography is essential[30].

Because NLE babies have an increased risk for developing autoimmune diseases later, a prospective long-term study should be done[29,30].

Conclusion

NLE should be suspected among neonates or young infants presenting with congenital heart block or skin rash with multi-system involvement despite a lack of concurrent maternal autoimmune diseases. Anti-Ro/SSA and/or anti-La/SSB are the most useful laboratory diagnosis. Most NLE patients without congenital heart block have relatively good prognosis. All mothers and NLE babies should be followed-up for the development of autoimmune diseases.

Potential conflicts of interest

None.

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โรคลูปัสในทารกแรกเกิด: การศึกษาย้อนหลัง 20 ปี

ศรีศุภลักษณ์ สิงคาลวณิช, วนิดา ลิ้มพงศานุรักษ์, สุทธิชา อู่เงิน

วัตถุประสงค์: เพื่อศึกษาอาการและอาการแสดงทางคลินิก ผลทางห้องปฏิบัติการ การดำเนินของโรค และการรักษาโรคลูปัสในทารกแรกเกิด

วัสดุและวิธีการ: เก็บข้อมูลย้อนหลังจากเวชระเบียนผู้ป่วยโรคลูปัสในทารกแรกเกิด ที่เข้ารับการรักษาในสถาบันสุขภาพเด็กแห่งชาติมหาราชินีตั้งแต่เดือนมกราคม พ.ศ. 2536 ถึง เดือนธันวาคม พ.ศ. 2556 โดยมีเกณฑ์การวินิจฉัย คือ อาการแสดงทางคลินิกเข้าได้กับโรคลูปัสในทารกแรกเกิด และมีผลตรวจ antiRo/SSA หรือ antiLa/SSB ให้ผลบวก

ผลการศึกษา: มีผู้ป่วย 34 รายหญิง 22 ราย ชาย 12 ราย อายุที่มีอาการตั้งแต่แรกเกิดจนถึงอายุ 60 วัน โดยผู้ป่วย 32 ราย (94.1%) เริ่มแสดงอาการก่อนอายุ 1 เดือน ค่า median ของอายุที่ได้รับการวินิจฉัยคือ อายุ 21 วัน อาการทางคลินิกที่พบความผิดปกติ ได้แก่ ระบบผิวหนัง ระบบตับและทางเดินน้ำดี ระบบโลหิตและระบบหัวใจพบร้อยละ 88.2, 52.9, 50 และ 14.7 ตามลำดับ อาการทางระบบผิวหนัง ได้แก่ erythematous patch ร้อยละ 70, annular lesions ร้อยละ 36.6, petechiae ร้อยละ 26.6, raccoon eye ร้อยละ 26.6 และ telangiectasia ร้อยละ 20 อาการทางระบบตับและทางเดินน้ำดีพบ 18 ราย ได้แก่ transaminase enzyme เพิ่มขึ้นร้อยละ 100 ตับม้ามโต ร้อยละ 38.8 conjugated bilirubin เพิ่มขึ้นร้อยละ 22.8 อาการทางระบบโลหิตพบ 17 ราย ได้แก่ โลหิตจางร้อยละ 29.4 โลหิตจางร่วมกับเกร็ดเลือดต่ำร้อยละ 20.6 อาการทางระบบหัวใจพบน้อยที่สุด 5 ราย ได้แก่ complete heart block 4 ราย และ second degree arterioventricular block 1 ราย ผลการตรวจ antiRo/SSA ให้ผลบวก 31 ราย (91.1%) antiLa/SSB 20 ราย (58.8%) และ ตรวจพบทั้ง antiRo/SSA และ antiLa/SSB 18 ราย (52.9%) ผู้ป่วย 4 รายที่เป็น complete heart block ได้รับการรักษาโดยใส่ pacemaker ผู้ป่วย 11 ราย ได้รับยาคอร์ติโคสเตียรอยด์กิน เนื่องจากความผิดปกติทางผิวหนังรุนแรงและผลการทำงานของตับในเลือดผิดปกติไม่พบว่ามีผู้เสียชีวิต มารดาผู้ป่วยปกติ 24 ราย (72.7%) มีประวัติและอาการแสดงของโรค autoimmune 10 ราย (27.3%) ได้แก่ SLE 7 ราย autoimmune disease 3 ราย (8.8%) เมื่อติดตามผู้ป่วยพบว่ามารดา 7 รายที่ไม่มีอาการ ต่อมาแสดงอาการของ SLE ภายในระยะเวลา 3 ปี

สรุป: ควรคิดถึงโรคลูปัสในทารกแรกเกิดที่มีอาการ complete heart block ผื่นผิวหนัง อาการทางตับและทางเดินน้ำดี อาการทางโลหิต ถึงแม้ว่ามารดาจะไม่มีโรค autoimmune การเจาะเลือดเพื่อหา antiRo/SSA และ antiLa/SSB ช่วยในการวินิจฉัยโรคทารกที่ไม่มี complete heart block มีการพยากรณ์โรคที่ดี