

A 3-Day-Old Girl Referred From Her Pediatrician for Oral Ulcerations

Mary Lauren Neel, MD, Jeremy Kern, MD, Tova Ronis, MD

A 3-day-old girl was referred from her pediatrician for oral ulcerations. The patient was otherwise well appearing and afebrile. Her prenatal and antenatal courses were unremarkable, except for a failed routine hearing screen. The patient's examination was notable for several yellowish ulcers on erythematous bases located on her anterior tonsillar pillars. The patient also had a right coloboma and a II/VI systolic ejection murmur. Laboratory analyses revealed a traumatic lumbar puncture with 182 000 red blood cells and 808 white blood cells, as well as a complete blood count that showed thrombocytopenia and leukocytosis. During the patient's hospitalization, she developed a new facial rash. Her physical examination findings, along with her diagnostic evaluation and hospital course, ultimately led to 2 surprising diagnoses elaborated on in this case discussion.

abstract

CASE HISTORY WITH SUBSPECIALTY INPUT

Dr Mary Lauren Neel (Pediatrics, Chief Resident):

A 3-day-old girl was referred to the emergency department from her pediatrician for oral ulcerations. In the pediatrician's office, she had several yellow shallow patches/ulcers on her soft palate. The infant was otherwise afebrile and well appearing. She was born at 40.3 weeks' gestation to a 41-year-old G₄P₂₀₂₂ mother via spontaneous vaginal delivery, with a birth weight of 2750 g. Her mother had no significant past medical history; and prenatal laboratory analyses, including group B *Streptococcus*, were negative. Although the mother denied a history of herpes simplex virus (HSV), she did not undergo HSV laboratory testing during pregnancy. The patient's prenatal, birth, and postnatal courses were unremarkable, except for a failed auditory brainstem-response hearing screen on the left side. Of note, the patient had undergone a hearing screen as part of a state-mandated program, not due to

any specific concerns. The patient had been referred to audiology to retest her hearing after discharge.

Upon examination in the emergency department, the patient's vital signs were normal for her age, and she was well appearing. The oral ulcerations were described as yellowish ulcers on erythematous bases located on anterior tonsillar pillars. The patient was noted to have a right coloboma and a II/VI systolic ejection murmur with an otherwise normal examination.

Dr Agrawal, as a Pediatric Emergency Medicine physician, can you share your initial thoughts about this patient's differential diagnosis for her chief complaint? What would be your first steps in her diagnostic evaluation and management?

Dr Dewesh Agrawal (Pediatric Emergency Medicine):

My initial differential diagnosis would include aphthous ulcers, herpetic gingivostomatitis, neonatal lupus erythematosus (NLE), neonatal syphilis, congenital cytomegalovirus

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Dr Neel conceptualized the case presentation and drafted the initial manuscript; Drs Kern and Ronis assisted with conception of the case presentation and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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FIGURE 1
Variations of prominent antihelices noted in association with CHARGE syndrome. Reprinted with permission from Lalani SR, Hefner MA, Belmont JW, et al. CHARGE Syndrome. 2006 Oct 2 [Updated 2012 Feb 2]. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews*. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK1117/>. Copyright 1993-2015 University of Washington, Seattle, WA.¹

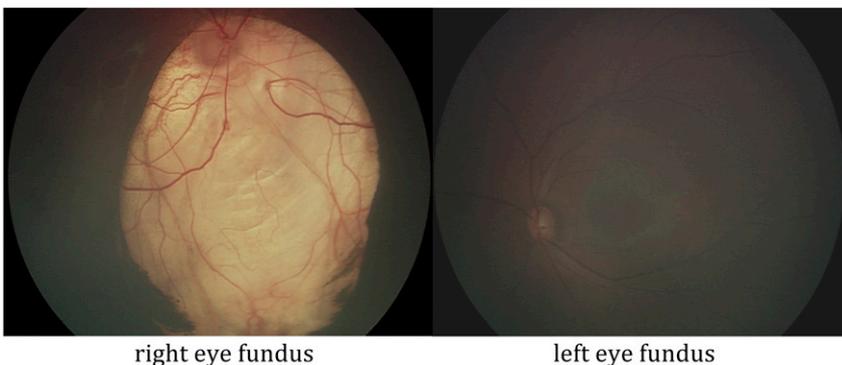


FIGURE 2
Our patient's left and right fundus photographs. The left photograph shows her extensive chorioretinal coloboma, and the right photograph shows her normal fundus. Photo courtesy of Dr Heather De Beaufort, MD, Children's National Medical Center, Washington, DC.



FIGURE 3
NLE rash as shown on our patient. Photo courtesy of Dr Scott Norton, MD, MPH, Children's National Medical Center, Washington, DC.

important diagnosis to exclude. CMV is on the list because of the failed hearing screen. I am not quite sure how the patient's additional physical examination findings correlate with her chief complaint of oral ulcers. Coloboma and heart defects are the "C" and "H" of coloboma, congenital heart disease, choanal atresia, developmental and growth retardation, genitourinary anomalies, and ear malformations (CHARGE) syndrome, but I do not think that relates to her chief complaint .

In terms of initial evaluation, I would ask as many faculty colleagues as I could to evaluate the ulcers to see if they had ever seen similar lesions. I'd test for HSV, varicella zoster virus, and CMV in conjunction with infectious disease recommendations. I'd obtain a complete blood count to assess white blood cell (WBC) and platelet count and alanine aminotransferase/alanine transaminase to assess for disseminated HSV. Because NLE is on the differential, I'd perform a complete skin examination and rule out heart block with a 12-lead electrocardiogram (ECG).

Dr Neel:

Would you perform a full sepsis workup on this well-appearing, afebrile infant in the emergency department?

(CMV), and varicella zoster virus. Of that list, aphthous ulcers is a

diagnosis of exclusion and herpetic gingivostomatitis is the most

Dr Agrawal:

I would not necessarily jump to complete a full sepsis workup on this well-appearing, afebrile infant. In the literature on febrile infants, well appearance does not obviate the need for a sepsis evaluation, but the infant in this case is afebrile. However, I would certainly discuss this case with my infectious disease colleagues. If there were serious concern that this was HSV and the child needed acyclovir pending negative testing, or if she were unable to eat, appeared ill, or developed a fever, I would admit her to the hospital.

Dr. Neel:

Dr DeBiasi, you are consulted on this patient in the emergency department. Would you recommend a full sepsis workup for this patient? Are there any other etiologies on your initial differential for this patient?

Dr Roberta DeBiasi (Pediatric Infectious Disease):

As Dr Agrawal said, HSV is the “can’t miss” diagnosis in this patient. Any child in this age group (birth to 6 weeks of age) with mucosal lesions could have neonatal HSV and possible skin, eye, mouth (SEM) presentation; and patients with SEM HSV can certainly be afebrile upon admission. As such, I would recommend that this patient be admitted for full evaluation for neonatal HSV, which includes lumbar puncture (LP) for cerebrospinal fluid (CSF) cell counts and CSF HSV polymerase chain reaction (PCR), as well as mucosal surface swabs for HSV culture (swabs from conjunctivae, nasopharynx, mouth, and anus), and blood for HSV PCR and alanine transaminase. Intravenous acyclovir should be initiated while this evaluation is pending. Of all children presenting with neonatal HSV SEM presentation without obvious central nervous system involvement, 30% may have PCR-proven HSV in their spinal fluid. The other most likely infectious

etiologies of oral ulcerations in this infant include syphilis or enterovirus. In any infant presenting with unusual findings, we have to consider all congenital infections, but oral ulcerations are not a typical finding in other congenital infections. CMV does not present with oral mucosal lesions but must still be considered given that it is the most common congenital infection and the most common cause of sensorineural hearing loss.

Dr Neel:

What tests do we order to rule out these infections?

Dr DeBiasi:

HSV PCR is the test of choice for CSF. For surface swabs, including oral lesions, HSV culture remains the test of choice. The performance of PCR assay on skin and mucosal specimens from neonates has not been studied; if used, surface PCR assays should be performed in addition to (not instead of) the gold-standard surface culture.²

In addition to testing for HSV, a rapid plasma reagin should be sent on the infant and a venereal disease research laboratory test should be sent on CSF to evaluate for syphilis. An enterovirus PCR could also be run on both infant blood and CSF. The enterovirus PCR tests for coxsackie, echovirus, and enteroviruses. To make a diagnosis of congenital CMV, urine culture or urine PCR testing must be done in the first 3 weeks of life, so as to distinguish these infants from those who acquire postnatal CMV infection.

Dr Neel:

The patient underwent a full sepsis workup, including an LP in the emergency department and was started on ampicillin, cefotaxime, and acyclovir. The LP was traumatic, with 182 000 red blood cells (RBCs) and 808 WBCs. She also had a complete blood count that showed

thrombocytopenia and leukocytosis (Table 1 and 2).

Dr Agrawal, would you be concerned that the large number of RBCs in the patient’s CSF might be due to HSV infection in the brain?

Dr Agrawal:

HSV meningoencephalitis should always be in the differential of a neonate who presents with CSF pleocytosis. The presence of a significant number of RBCs raises the concern for HSV-associated hemorrhagic necrosis of the brain and meninges. However, given this patient’s normal mental status at the time of the LP, she was probably not having hemorrhagic necrosis of her brain, which would typically present with altered mental status and possibly seizures. Of course, you should still start acyclovir empirically pending the results of the HSV PCR. Nevertheless, the clinical picture presented here is inconsistent with fulminant central nervous system HSV-associated hemorrhagic necrosis; it is most likely a “traumatic” LP. There are varying schools of thought in using a ratio of 500:1 RBCs to WBCs to “correct” for a traumatic LP. The bottom line is that these corrections are not always reliable.^{3,4}

Dr Neel:

The patient remained stable, and she was admitted to the general pediatrics team. A disseminated intravascular coagulation panel was ordered due to the patient’s thrombocytopenia and was unremarkable.

Dr. Greenberg, what do you make of the patient’s thrombocytopenia?

Dr Jay Greenberg (Pediatric Hematology-Oncology):

The overriding question in thrombocytopenia is whether it is due to increased destruction or decreased production. This well-appearing newborn’s

thrombocytopenia could be infectious versus immune-mediated. Rarely, bone marrow failure syndromes such as genetic conditions or metabolic disease, can also present as thrombocytopenia in newborns.

Increased destruction is more likely, especially if the child appears ill, and should be screened for with cultures and a disseminated intravascular coagulation panel. In a well-appearing child, I would also screen for prenatal viral infections, in particular CMV or HSV. In immune destruction, one would evaluate for the various types of idiopathic thrombocytopenic purpura (ITP) seen in newborns: alloimmune and maternal ITP.

The first step is to evaluate the mother's platelet count. If the mother's platelet count is low, the diagnosis is maternal ITP with maternal antibodies passed to the infant, leading to thrombocytopenia in the infant. If the mother's platelet count is normal, the next step is to order maternal serum testing for the most common forms of alloimmune thrombocytopenia. Common etiologies include maternal absence of a common platelet antigen like Pla-1 or because the mother has high titers of anti-HLA antigen antibodies from a previous pregnancy. In both of these cases, the mother's immune system identifies the infant's platelets as foreign and attacks them, leading to thrombocytopenia in the infant.

Dr Neel:

Dr Smpokou, you are consulted by the pediatrics team given the patient's coloboma, murmur, failed hearing screen, and now thrombocytopenia. Are there any genetic or metabolic diagnoses you are considering for this patient, which may or may not be related to her chief complaint of oral ulcerations?

Dr Patroula Smpokou (Pediatric Genetics and Metabolism):

This patient has some elements of CHARGE syndrome given her coloboma, murmur, and possible hearing loss (failed hearing screen). However, the 4 primary diagnostic criteria for CHARGE association are ocular coloboma, choanal atresia/stenosis, cranial nerve dysfunction, and characteristic ear malformation(s) with prominent antihelix and malformed lobe (Fig 1). A more common syndromic cause of ocular coloboma is Kabuki syndrome; however, most isolated colobomas are nonsyndromic.

Dr Neel:

Dr Smpokou, does CHARGE syndrome have any hematologic abnormalities?

Dr Smpokou:

No, typically CHARGE does not have associated hematologic abnormalities and so coexisting or alternative causes should be sought. I also cannot explain the child's oral ulcerations with the rest of her physical examination findings in a syndromic association.

Dr Neel:

Dr De Beaufort, what is the standard workup for children with colobomas?

Dr Heather De Beaufort (Pediatric Ophthalmology):

Evaluation for children with colobomas includes a complete physical examination including thorough cardiac examination, a renal ultrasound, at least state-mandated audiology testing, and a brain MRI only if the patient has developmental delay. Any abnormalities on physical examination or initial workup would guide further testing to evaluate for syndromic association or additional complications.⁵

Dr Neel:

Is there anything else we should know about patients with colobomas?

Dr De Beaufort:

Only that some patients, such as this one, can even have leukocoria due to very large colobomas.

An isolated iris coloboma generally will have minimal impact on vision. Iris colobomas may be associated with a lens coloboma due to a defect in the ciliary processes directly behind the iris, which can lead to astigmatism and/or early cataracts.⁶

Chorioretinal colobomas can have variable impact on vision, ranging from 20/20 vision to no light perception. As a general rule, if a chorioretinal coloboma is in the inferior retina and does not involve the macula, the visual prognosis is good. Some children also have optic nerve involvement in the coloboma, which can have a varied impact on the vision that is difficult to predict on the basis of examination. Some patients with large optic nerve colobomas can have intact vision, and some with mild-appearing colobomatous nerves can have poor vision (Fig 2).⁶

Dr Neel:

On hospital day 3, the patient's CSF HSV PCR and surface swabs returned negative. Her CSF bacterial cultures were also negative. Her oral ulcers had resolved, and she was still afebrile and feeding well. The patient had an ECG given her murmur, which showed a small ventricular septal defect (VSD). Chest radiograph was normal. Her liver function tests, including alanine aminotransferase/alanine transaminase, albumin, total protein, and total and direct bilirubin, were normal; and she continued without hepatosplenomegaly on examination. Given that the patient continued to look well clinically and HSV testing was negative, acyclovir

TABLE 1 Laboratory Data

Test	Reference Range	Patient Results
WBCs, K/mcL	8.2–14.6	37.4
Hemoglobin, g/dL	13.4–20.0	20.7
Hematocrit, %	39.6–57.2	57.5
Platelets, K/mcL	144–449	40
Differential, %		
Segmented neutrophils	23–58	63
Band neutrophils	0–1	2
Lymphocytes	28–55	11
Monocytes	8–13	12
Sodium, mmol/L	131–144	135
Potassium, mmol/L	3.2–5.7	3.6
Chloride, mmol/L	97–108	106
Carbon dioxide, mmol/L	13–21	19
Urea nitrogen, mg/dL	1–13	9
Creatinine, mg/dL	0.7–1.2	<0.1
Glucose, mg/dL	47–110	89
Urine		
WBCs, high-power field	<6	0
RBCs, high-power field	<3	3
Nitrite, mg/dL	Negative	Negative
Leukocyte esterase	Negative	Negative
CSF		
WBCs, n/mcL	0–20	808
RBCs, n/mcL	0	182 000
Glucose, mg/dL	41–84	42
Protein, mg/dL	15–153	Test credited

was discontinued. Antibiotics were continued given the elevated WBC count in the CSF.

By hospital day 9, the patient had completed her antibiotics and had developed a scaly plaque on her eyebrow. In addition, her rapid plasma reagin, Epstein-Barr virus titers, and fluorescent treponemal antibody, toxoplasmosis, CMV, and rubella antibodies all returned negative, ruling out many of the congenital and viral infections on our initial differential.

Dr Kirkorian, what is your differential diagnosis for this rash?

Dr Yasmine Kirkorian (Pediatric Dermatology):

The differential for a scaly facial rash in this patient includes seborrheic

TABLE 2 Pending Microbiology

Aerobic blood culture
Surface HSV PCR
Urine culture
CSF culture
CSF HSV PCR

dermatitis, atopic dermatitis, infectious etiologies including tinea faciei and NLE. The striking periocular distribution of scaly annular patches and plaques is highly concerning for NLE. Periorbital erythema (referred to as “raccoon eyes,” “owl eyes,” or “eye-mask”) is another classic finding of NLE.⁷ Cutaneous manifestations frequently occur on sun-exposed sites such as the face but may occur on sun-protected areas or may be present at birth. NLE is an important manifestation of risk for the patient’s mother because ~50% of mothers are asymptomatic at the time of delivery.⁸

Dr Neel:

Dr Ronis, how do we diagnose NLE?

Dr Tova Ronis (Pediatric Rheumatology):

The diagnosis of NLE is established on the basis of the presence of classic clinical findings in conjunction with the finding of positive associated antibodies. It is often easier to order

the antibody tests on the mother. If they are negative, there is no need to order them on the infant. If they are positive, they can be presumed to be positive in the infant.

Dr Neel:

In this case, our patient’s Sjögren syndrome–related antigen A (SS-A) did return positive. The presence of the positive SS-A antibodies, along with her physical and laboratory findings, confirmed the diagnosis of NLE in this infant.

Dr Krishnan, what cardiac manifestations should we be concerned about in NLE?

Dr Anita Krishnan (Pediatric Cardiology):

The cardiac effects of the SS-A antibody typically occur in utero between 16 and 25 weeks’ gestation.^{9,10} NLE is a misnomer, because mothers carrying anti-SS-A (anti-Ro) antibodies can have systemic lupus erythematosus (SLE), Sjögren syndrome, mixed connective tissue disease, or be completely asymptomatic. Cardiac findings consistent with NLE include heart block or cardiomyopathy, but less well-known diseases such as arrhythmias, structural heart disease, and endocardial fibroelastosis can also occur.^{10–13} These antibodies cross the placenta and, in a small number of infants, trigger an inflammatory myocarditis that ultimately leads to fibrosis of the atrioventricular node. Once this happens, the process is thought to be irreversible. If the infants are born with a normal ECG, it is unlikely that they will develop heart block; however, if they are born with first-, second-, or third-degree heart block, it can progress in the first year because the infant still has circulating SS-A antibodies for ~6 months.

Dr Neel:

Fortunately, our patient had a normal ECG at birth. As such, she did not

require or receive additional ECG screening.

Dr Smpokou, what about our patient's other findings (ie, her coloboma, failed hearing screen, and VSD)?

Dr Smpokou:

These findings are not explained by her NLE. The patient was followed closely in genetics clinic given her multiple congenital anomalies. A microarray looking for microdeletions and microduplications returned normal. At 15 months of age, Noonan syndrome (NS) testing was sent given the patient's mild developmental delay, poor growth, VSD, and mild facial dysmorphism. The patient was diagnosed with NS caused by a missense *PTPN11* gene mutation. Ocular colobomas are a rarely reported malformation in NS; however, the most likely explanation is that it is part of her underlying NS.

The patient's auditory brainstem-response hearing screen was retested during her initial admission. The results indicated mild bilateral hearing loss. The patient had intermittent repeat outpatient testing, all of which was suboptimal given the lack of cooperation or awake state. However, repeat testing at 20 months of age revealed normal hearing bilaterally.

FINAL DIAGNOSIS AND DISCUSSION: NLE AND ASSOCIATION BETWEEN LUPUS AND NS

Dr Ronis:

This case was challenging in that the patient had more findings than are typically seen in NLE. However, autoimmune cytopenia and skin rash are classic features of this disorder and, along with the presence of the positive SS-A (Ro) antibodies, confirmed the diagnosis. Although palatal ulcers are commonly seen in pediatric and adult-onset SLE, oral ulcers have not been reported in NLE.

The development of the classic rash is what led the team to consider this diagnosis for our patient.

With further follow up, we were later able to explain the patient's coloboma and VSD as likely secondary to her NS. The failed hearing screen was likely due to suboptimal testing rather than true hearing deficiency. This patient's myriad of signs and symptoms required a true multidisciplinary team approach and time to uncover her 2 diagnoses. Still, the true etiology of her initial chief complaint, the ulcers, is unknown.

NLE is due to passive transfer of maternal antibodies to a developing fetus. The maternal antibodies include SS-A (Ro) antibody, Sjögren syndrome-related antigen B (La) antibody, and rarely, other autoantibodies. Many pregnant mothers with these antibodies do not have children with NLE, and most mothers of infants with NLE were unaware that they had positive antibodies before having an affected child. Clinical manifestations of NLE include cardiac, cutaneous, hematologic, and hepatic findings.

Cardiac

Cardiac manifestations of NLE lead to the most morbidity and mortality and are associated with anti-SS-A antibodies. Congenital heart block (CHB) is the most common complication. Most often, CHB is diagnosed in utero when fetal bradycardia is detected. An estimated 1 of 14 000 live births are complicated by CHB, and 90% of cases are due to the maternal autoantibodies causing NLE. This is due to degradation of the atrioventricular node, which becomes replaced by fibrotic tissue. Autoimmune CHB is frequently detected by 24 weeks' gestation. By the time fetal bradycardia is detected, the damage can be irreversible. Advanced cases of second- or third-degree heart block may be associated with hydros fetalis and adverse

fetal outcomes. Mothers known to have pathogenic antibodies can be followed early in pregnancy with serial Doppler echocardiography to measure the P-R interval to assess for first-degree heart block. It is controversial whether maternal corticosteroid therapy during pregnancy improves fetal outcomes. Despite intervention, many children with CHB ultimately require a pacemaker.¹⁴

Cutaneous

The rash associated with cutaneous NLE is photosensitive and typically involves the face and scalp. It often occurs around the eyes as periorbital erythema, referred to as "raccoon distribution," and rarely occurs in a malar distribution. It has the appearance of an annular erythematous scale with central clearing and may feature bullous lesions. The rash may resemble primary HSV, erythema multiforme, or Langerhans cell histiocytosis. Reports vary given delays in recognition and the transient nature of the rash, but studies report that 15% to 70% of children with NLE have a rash.^{15,16} The rash typically develops around 6 weeks of life, and new lesions continue to develop for several months. Generally, the rash stops developing after 6 months of age when maternal antibodies disappear from the infant's circulation. The lesions are transient. The treatment of cutaneous NLE is reassurance and photoprotection. Mild topical corticosteroid cream may hasten the resolution of rash (Fig 3).¹⁴

Hematologic

Usually hematologic manifestations occur in conjunction with other signs of NLE but rarely can occur in isolation. Thrombocytopenia occurs most commonly, but anemia, neutropenia, and pancytopenia can also be seen. There have been reports of neonatal thrombosis and aplastic anemia associated with maternal

antibody transfer. Hematologic manifestations of NLE tend to resolve spontaneously over several weeks without treatment. If there are severe complications such as bleeding, high-dose corticosteroids or intravenous immunoglobulin may be used.¹⁴

Hepatic

Hepatomegaly and transaminitis can be seen in up to 25% of infants with NLE, either in isolation or in conjunction with other stigmata. These abnormalities generally self-resolve, although they can rarely lead to hepatic failure. Liver biopsy is not usually indicated.¹⁴

Other Manifestations

There have been isolated case reports of neurologic manifestations. Chondrodysplasia punctata (group of skeletal dysplasias), congenital nephrotic syndrome, and Turner syndrome have all been reported in patients with NLE.¹⁴ If maternal antithyroid antibodies are present, they may cross the placenta and cause thyroid disease in the newborn. The constellations of findings seen in our patient have not been reported with this disease.

Because maternal antibodies generally resolve, the features of NLE are transient except for CHB, which is permanent. Infants with NLE may be at an increased risk of developing an autoimmune disease later in life, but that risk is equivalent to that of children without NLE born to mothers with SLE.

Mothers without a diagnosed autoimmune disease are at risk of developing one in the future and should be counseled to follow up with their doctor for screening for autoimmune diseases. Families should be counseled about the risk of recurrence of NLE in future pregnancies. There is an estimated recurrence rate of CHB of 8% to 25% in subsequent pregnancies.¹⁴ In our case, the mother did follow up with adult rheumatology and was

diagnosed with lupus. Although there have been reported associations between NS and autoimmune diseases including 5 cases of NS and SLE, our literature review did not reveal any other reported cases of patients with NS and NLE.¹⁷⁻²¹

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ABBREVIATIONS

CHARGE: coloboma, congenital heart disease, choanal atresia, mental and growth retardation, genital anomalies, and ear malformations and hearing loss
CHB: congenital heart block
CMV: cytomegalovirus
CSF: cerebrospinal fluid
ECG: electrocardiogram
HSV: herpes simplex virus
ITP: idiopathic thrombocytopenic purpura
LP: lumbar puncture
NLE: neonatal lupus erythematosus
NS: Noonan syndrome
PCR: polymerase chain reaction
RBC: red blood cell
SEM: skin, eye, mouth
SLE: systemic lupus erythematosus
SS-A: Sjögren syndrome–related antigen A
VSD: ventricular septal defect
WBC: white blood cell

REFERENCES

1. Lalani SR, Hefner MA, Belmont JW, et al. CHARGE syndrome. In: Pagon RA, Adam MP, Ardinger HH, eds. *GeneReviews*. Seattle, WA: University of Washington; 2006. <http://www.ncbi.nlm.nih.gov/books/NBK1117/>. Accessed May 10, 2016
2. American Academy of Pediatrics. Herpes Simplex. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*, 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:432–445
3. Greenberg RG, Smith PB, Cotten CM, et al. Traumatic lumbar punctures in neonates: test performance of the cerebrospinal fluid white blood cell count. *Pediatr Infect Dis J*. 2008;27(12):1047–1051
4. Srinivasan, L, Harris MC, Shah SS. Lumbar puncture in the neonate: challenges in decision making and interpretation. *Semin Perinatol*. 2012;36(6):445–453
5. Huynh N, Blain D, Glaser T, et al. Systemic diagnostic testing in patients with apparently isolated uveal coloboma. *Am J Ophthalmol*. 2013;156(6):1159–1168.e4
6. Chang L, Blain D, Bertuzzi S, Brooks BP. Uveal coloboma: clinical and basic science update. *Curr Opin Ophthalmol*. 2006;17(5):447–470
7. Paller AS, Mancini AJ. *Hurwitz Clinical Pediatric Dermatology*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2011
8. Rivera TL, Izmirly PM, Birnbaum BK, et al. Disease progression in mothers of children enrolled in the Research Registry for Neonatal Lupus. *Ann Rheum Dis*. 2009;68(6):828–835
9. Buyon JP, Hiebert R, Copel J, et al. Autoimmune-associated congenital heart block: demographics, mortality, morbidity and recurrence rates obtained from a national neonatal lupus registry. *J Am Coll Cardiol*. 1998;31(7):1658–1666
10. Hornberger LK, Al Rajaa N. Spectrum of cardiac involvement in neonatal lupus. *Scand J Immunol*. 2010;72(3):189–197
11. Costedoat-Chalumeau N, Amoura Z, Villain E, Cohen L, Piette JC. Anti-SSA/Ro antibodies and the heart: more than complete congenital heart block?

- A review of electrocardiographic and myocardial abnormalities and of treatment options. *Arthritis Res Ther.* 2005;7(2):69–73
12. Cuneo BF, Fruitman D, Benson DW, et al. Spontaneous rupture of atrioventricular valve tensor apparatus as late manifestation of anti-Ro/SSA antibody-mediated cardiac disease. *Am J Cardiol.* 2011;107(5):761–766
 13. Cuneo BF, Strasburger JF, Niksch A, Ovadia M, Wakai RT. An expanded phenotype of maternal SSA/SSB antibody-associated fetal cardiac disease. *J Matern Fetal Neonatal Med.* 2009;22(3):233–238
 14. Buyon JP, Lindsley CB, Silverman ED, et al. Neonatal lupus erythematosus. In: Cassidy JT, Petty RE, Laxer RM, Lindsley CB, eds. *Textbook of Pediatric Rheumatology*, 6th ed. Philadelphia, PA: Saunders Elsevier; 2011:361–372
 15. Cimaz R, Spence DL, Hornberger L, Silverman ED. Incidence and spectrum of neonatal lupus erythematosus: a prospective study of infants born to mothers with anti-Ro autoantibodies. *J Pediatr.* 2003;142(6):678–683
 16. Kobayashi R, Mii S, Nakano T, Harada H, Eto H. Neonatal lupus erythematosus in Japan: a review of the literature. *Autoimmun Rev.* 2009;8(6):462–466
 17. Lopez-Rangel E, Malleson PN, Lirenman DS, Roa B, Wiszniewska J, Lewis ME. Systemic lupus erythematosus and other autoimmune disorders in children with Noonan Syndrome. *Am J Med Genet A.* 2005;139(3):239–242
 18. Alanay Y, Balci S, Ozen S. Noonan syndrome and systemic lupus erythematosus: presentation in childhood. *Clin Dysmorphol.* 2004;13(3):161–163
 19. Amoroso A, Garzia P, Vadacca M, et al. The unusual association of three autoimmune diseases in a patient with Noonan syndrome. *J Adolesc Health.* 2003;32(1):94–97
 20. Lisbona MP, Moreno M, Orellana C, Gratacos J, Larrosa M. Noonan syndrome associated with systemic lupus erythematosus. *Lupus.* 2009;18(3):267–269
 21. Martin DM, Gencyuz CF, Petty EM. Systemic lupus erythematosus in a man with Noonan syndrome. *Am J Med Genet.* 2001;102(1):59–62

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