Congenital Hypothyroidism: Clues to an Early Clinical Diagnosis

Elmer S. Lightner, MD
Tucson, Arizona

Congenital hypothyroidism is clinically difficult to diagnose early in life. A review of the common signs and symptoms of this treatable disease is presented, and a case diagnosed on the third day of life is discussed. Until neonatal thyroid screening is generally available it behooves all physicians caring for newborns and young infants to have a high index of suspicion for this disease.

Laboratory screening for neonatal hypothyroidism has recently been proposed as a means of early detection of this potentially treatable cause of mental deficiency.[1-3] The incidence of congenital hypothyroidism is approximately 1 in every 6,000 births; a frequency three times more common than phenylketonuria. Previous studies of the development of infants with hypothyroidism have suggested a much better developmental and intellectual prognosis if therapy is initiated early in life (< 3 months of age). Thus, most authorities believe that early diagnosis and treatment of congenital hypothyroidism is extremely important.[4] *Clinical* diagnosis in the first few days or weeks of life may be very difficult, and screening programs offer a means of biochemically detecting subclinical disease and thus initiating early, effective treatment. Screening for neonatal hypothyroidism, however, probably will not be generally available in most hospitals for some time. It therefore behooves the physician seeing newborns and young infants to recognize that certain symptoms and signs may be quite suggestive of congenital hypothyroidism and should mandate laboratory testing to either rule in or rule out this disease.[5] This paper reports the clinical diagnosis of neonatal hypothyroidism in an infant on the third day of life, reemphasizing that a high index of suspicion for this disease can result in an early diagnosis.

From the Department of Pediatrics, Section of Endocrinology, University of Arizona, Tucson, Arizona. Requests for reprints should be addressed to Dr. Elmer S. Lightner, Department of Pediatrics, Section of Endocrinology, University of Arizona Health Sciences Center, Tucson, AZ 85724.

Case Report

A three-day-old, full term, white male infant was admitted to Arizona Medical Center with a condition tentatively diagnosed as congenital hypothyroidism. At birth, the infant weighed 2.8 kg and had Apgar scores of six and nine at one and five minutes. The mother's blood type was O-Rh negative; the infant's O-Rh positive. Direct and indirect Coombs tests were negative. He was discharged from the hospital at approximately 48 hours of age with a total bilirubin of 9.5 mg/100 ml. On the following morning, he returned to the physician's office with lethargy, a poor suck, abdominal distention, and a bilirubin of 17 mg/100 ml. He was noted to have a large anterior fontanelle and an open posterior fontanelle. Urine, blood, and cerebrospinal fluid cultures were obtained but were all subsequently sterile. The child was treated for potential sepsis after appropriate cultures were obtained.

Physical examination at the time of admission revealed a jaundiced, lethargic, hypotonic, white male infant with a poor cry and suck. Vital signs were normal. Significant positive findings included a large anterior fontanelle (3 × 4 cm), a large posterior fontanelle (Figure 1), a poorly developed nasal bridge, poor peripheral circulation (with marked mottling of the skin) (Figures 2A and B), a distended abdomen, and edema of the eyelids (Figure 2A) and hands. The thyroid gland was not palpable.

Admission laboratory values included a bilirubin of 18 mg/100 ml, hematocrit 47%, WBC 8,900/cu mm with a normal differential, and normal platelets. Thyroid function tests revealed the following values: serum thyroxine (T_4) 1.7 μg/100 ml, T_3 resin uptake 21% (normal 25 to 35%), and thyroid stimulating hormone (TSH) 695 μU/ml (normal 0 to 20 μU/ml). Roentgenograms revealed absence of both distal femoral epiphyses; no epiphyseal dysplasia was present, the skeletal maturation was that of a 34-week fetus.

Clinical Course

All cultures were subsequently negative and the antibiotics were discontinued; his bilirubin slowly fell. On the fifth day of life, levothyroxine therapy was started, 0.025 mg b.i.d. On several occasions, he became hypothermic and for the next seven to ten days he continued to feed poorly and had abdominal distention. He vomited bile-stained fluid intermittently; abdominal roentgenograms revealed no evidence of intestinal obstruction. On the eighth day, levothyroxine was increased to 0.05 mg b.i.d. A summary

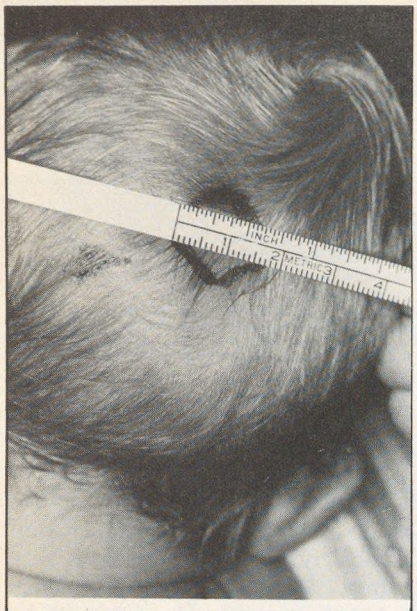

Figure 1. Open posterior fontanelle (1.7 × 1.7 cm).

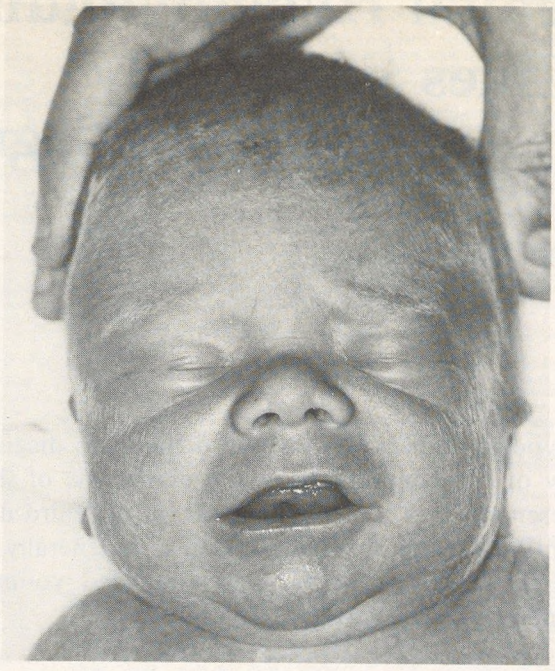

Figure 2A. Poorly developed nasal "bridge," mottled skin of anterior chest wall, and edema of eyelids.

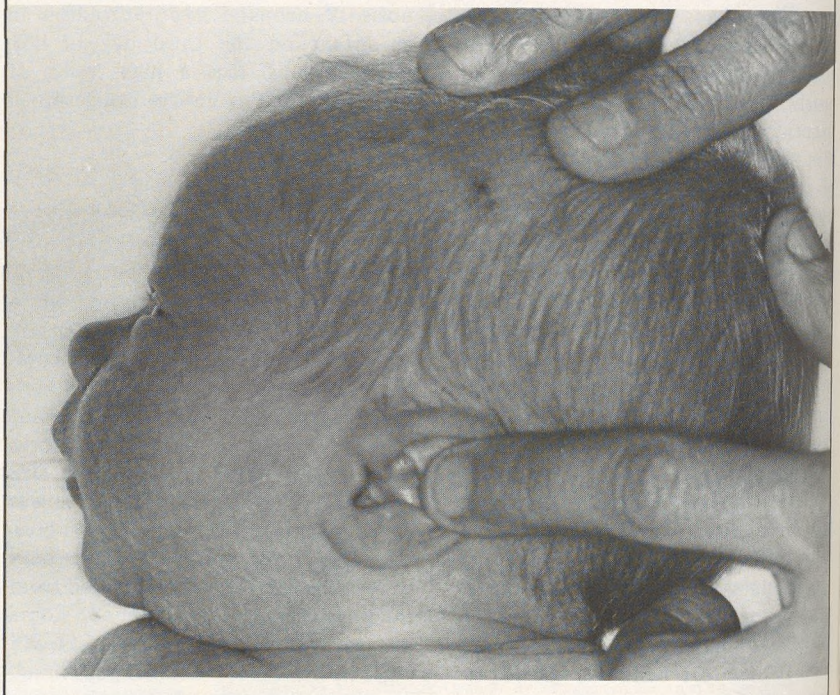

Figure 2B. Lateral showing poorly developed nasal bridge.

of his laboratory values are seen in Table 1. The infant slowly improved clinically and was discharged at 17 days of age on a levothyroxine dosage of 0.025 mg b.i.d.

Discussion

Smith et al have recently reviewed 15 cases of neonatal hypothyroidism.[5] The disease was diagnosed in three of the infants from clinical suspicion, confirmed by laboratory tests, before the age of ten days; it was detected in two others by neonatal thyroid screening, and in the other ten at one to five months of age, again by laboratory confirmation of suspicious clinical findings. In carefully reviewing the newborn records of these infants, it was apparent that certain symptoms and signs of hypothyroidism were often present in the neonate (Table 2). Although none of the infants had all of these signs and symptoms, they all had several of them; thus, the clinical index of suspicion should be elevated in all such infants. It is important to note that none of these infants had an umbilical hernia, a hoarse cry, or an enlarged tongue. These three findings have often been stated to be classical for congenital hypothyroidism; however, their appearance is often delayed beyond the first month of life, so awaiting these findings will significantly delay the diagnosis of this disease.

Two signs should be emphasized which should lead to a very high index of suspicion of congenital hypothyroidism. The first is a large, open posterior fontanelle in a term infant, since the posterior fontanelle is normally less than 0.5 cm in 97 percent of term infants.[6] In Smith's review, in all three instances where the size of the posterior fontanelle was specifically recorded, it was greater than 1 × 1 cm. Thus, it appears that this sign may be present in most, if not all, hypothyroid infants.

Table 1. Thyroid Function Tests and Therapy

Day of Life	T_4	T_3RU	T_3RIA	TSH	Therapy
3rd	1.7 μg/100 ml*	21%	67 ng/100 ml†	695	–
5th	–	–	–	–	Thyroxine 0.025 mg b.i.d.
10th	–	–	–	–	Thyroxine 0.05 mg b.i.d.
12th	8.0 μg/100 ml	–	132 ng/100 ml	–	–
20th	9.1 μg/100 ml	–	163 ng/100 ml	–	Thyroxine 0.025 mg b.i.d.

Normal for 3 days of age: *T_4 (11.5-21.5 μg/100 ml) †T_3RIA (100-740 ng/100 ml)

Table 2. Clues to Neonatal Hypothyroidism

	Smith	Our Infant
Gestation > 42 weeks	7/15	No
Birth weight > 4 kg	4/15	No
Large posterior fontanelle (> 0.5 cm)	5/5*	Yes
Respiratory distress	5/15	No
Hypothermia (< 95°)	5/14	Yes
Peripheral cyanosis (excessive mottling)	5/15	Yes
Hypoactivity, lethargy	4/15	Yes
Poor feeding	6/15	Yes
Lag in stooling > 20 hours	5/15	No
Abdominal distention	7/15	Yes
Vomiting	6/15	Yes
Icterus > 3 days	11/15	Yes
Edema	8/15	Yes
Poorly developed nasal bridge	2/15	Yes

*Specific information recorded in only five of the cases

Secondly, the "scooped out" appearance or failure of development of the nasal bridge is common in infants with congenital hypothyroidism. This is well illustrated in Figures 2A and B, and is also noted in the picture in Smith's article of the infant whose illness was diagnosed clinically at eight days of age.

Initially, our house officers were quite concerned that the infant had sepsis because of his jaundice, lethargy, and poor suck – symptoms common to both neonatal sepsis and congenital hypothyroidism. Later, after all cultures were reported as negative, his persistent abdominal distention and bile-stained vomiting led them to suspect obstruction of the gastrointestinal tract; these symptoms subsided after several days of thyroxine. Thus, congenital hypothyroidism should be considered in the differential diagnosis of any infant with signs and symptoms of sepsis or intestinal obstruction.

In summary, a review of Table 2 will refresh the physician's memory of the *very* early signs and symptoms of congenital hypothyroidism. Until this disease is routinely screened for in all hospitals, the physician caring for newborns must make a conscious effort to diagnose this disease in the suspect neonate.

References

1. Dussault JH, Coulombe P, Laberge C, et al: Preliminary report on a mass screening program for neonatal hypothyroidism. J Pediatr 86:670, 1975
2. Klein HA, Agustin AV, Foley TP Jr: Successful laboratory screening for congenital hypothyroidism. Lancet 2:77, 1974
3. Recommendations for screening programs for congenital hypothyroidism: A report of a committee of the American Thyroid Association. J Pediatr 89:692, 1976
4. Klein AH, Meltzer S, Kenny FM: Improved prognosis on congenital hypothyroidism treated before age three months. J Pediatr 81:912, 1972
5. Smith DW, Klein AM, Henderson JR, et al: Congenital hypothyroidism: Signs and symptoms in the newborn period. J Pediatr 87:958, 1975
6. Popich GA, Smith DW: Fontanels: Range of normal size. J Pediatr 80:749, 1972