CASE REPORT

Spontaneous improvement in sensorineural hearing loss developed as a complication of neonatal hyperbilirubinemia

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Abstract

Icterus neonatorum, or neonatal jaundice, is defined as a total serum bilirubin level above 5mg/dl. Acute bilirubin encephalopathy and kernicterus are known to be the two major complications associated with it, resulting in neurotoxic effects, including sensorineural hearing loss, hypotonia, delayed motor skills and intellectual deficits. We report two similar cases of neonatal jaundice requiring exchange transfusion that subsequently developed sensorineural hearing loss. Follow-up at the end of 1year revealed spontaneous recovery of hearing with normal speech. This report aims at increasing awareness of this condition among physicians to allow early detection of risk factors and prompt management and follow-up.

Keywords: Neonatal hyperbilirubinaemia, Sensorineural hearing loss, Kernicterus, Exchange transfusion.

Introduction

Icterus neonatorum, or neonatal jaundice, is defined as a total serum bilirubin level above 5mg/dl. Hyperbilirubinaemia typically results from the deposition of unconjugated bilirubin, manifested in skin and mucus membranes.[1] Hyperbilirubinaemia is one of the commonest reasons for morbidity in the neonatal period, occurring in around 60% of term newborn babies by 48-72 hours of age, with 5-10% requiring intervention for pathological jaundice.[2] One study defined pathological jaundice as serum bilirubin concentration being more than 17mg/dl in full-term infants.[3] Neonatal jaundice remains the most common health issue in the neonatal age group, affecting approximately 50% of term and 75% of pre-term infants, with hyperbilirubinaemia in pre-terms being more severe and having a much worse course than in full-term neonates.[1,4]

Incidence of hyperbilirubinaemia varies with ethnicity and geography, with incidence being high in East Asians, native Americans and Greek islanders, and low in African Americans. Incidence is higher in populations living at high altitudes.[5] According to a study done in a neonatal unit in Karachi, hyperbilirubinaemia is the third leading cause requiring admission for neonates.[6]

Causes of pathological jaundice in newborns include increased production of bilirubin, deficiency of hepatic uptake, impaired conjugation of bilirubin, and increased enterohepatic circulation of bilirubin.[2]

The major risk factors associated with pathological jaundice are worth taking a look at (Table-1). Of all these risk factors, prematurity appears to be the most significant. One study stated prematurity to be a significant risk factor, and a basis for increased biological vulnerability to risk of developing bilirubin-induced neurotoxicity.[7]

There are two major complications of hyperbilirubinaemia: acute bilirubin encephalopathy, and kernicterus. A research done in National Institute of Child Health (NICH), Pakistan, reported incidence of kernicterus in hyperbilirubinaemic premature infants to be 2-16%.[1] Of them, 75% or more of such infants died and 80% of affected survivors were reported to have bilateral choreoathetosis with involuntary muscle spasms, and other neurodevelopmental abnormalities, such as sensorineural hearing loss, hypotonia, tremors, ballismus, delayed motor skills, and rarely, intellectual deficit.[1,8] Increased concentration of bilirubin in the brain requiring exchange transfusion along with early age of onset of hyperbilirubinaemia increasing the duration of exposure to bilirubin are important determinants of the neurotoxic effects of bilirubin.[2,9] The auditory pathway is one of the most sensitive parts of the nervous system to this toxic agent, thus, neonatal hyperbilirubinaemia is a common cause of early onset sensorineural hearing loss.[10]

We report two similar cases of infants with bilirubin levels that approached thresholds for exchange transfusion and subsequently developed sensorineural hearing loss as a consequence of neonatal hyperbilirubinaemia. To the best of our knowledge, these are the first reported cases from Pakistan that showed some spontaneous improvement over time in sensorineural hearing loss acquired as a complication of neonatal hyperbilirubinaemia.

Case Report

The two cases being presented relate to the Aga Khan University Hospital (AKUH), Karachi, were they came

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separately between July 2012 and July 2013. Written consent was obtained from the parents of the patients for sharing our experience with the two babies. Maternal and neonatal risk factors present in the two cases were noted separately (Tables-2 and 3).

Our first patient was a girlborn pre-term at 34 weeks of gestation after an uneventful pregnancy. Birth weight was 2.8kg. No neonatal problems or trauma during normal vaginal delivery resulting in cephalohematoma or ecchymoses was reported. However, she developed unconjugated hyperbilirubinaemia on second day of life and the bilirubin level reached peak of 33.6mg/dl (indirect=32.3; direct=1.4) on sixth day of life. There was no family history of any genetic, enzymatic or metabolic defects. She required 2 days of phototherapy and 1 exchange transfusion. Lab investigations, including haemoglobin (Hb), reticulocyte count and throid stimulating hormone (TSH) was within

Table-1: Risk factors associated with neonatal hyperbilirubinaemia.

Maternal Factors	Perinatal Factors	Neonatal Factors
1. Race or ethnic group	**1. Birth trauma**	**1. Prematurity**
	2. Genetic disorders	
Asian	Cephalohematoma	a) Familial disorders of conjugation
Native American	Ecchymoses	Gilbert's Syndrome
Greek Islander		Crigler-Najjar Syndrome types I and II
2. Complications during pregnancy	**2. Infections**	b) Other enzymatic defects
	Bacterial	Glucose-6-phosphate dehydrogenase deficiency
Diabetes mellitus	Viral	Pyruvate kinase deficiency
Rh incompatibility	Protozoal	Hexokinase deficiency
ABO incompatibility		c) Erythrocyte structural defects
		Spherocytosis
		Elliptocytosis
3. Breast-feeding jaundice (late-onset)		**3. Polycythaemia**
		4. Drugs
		Streptomycin
		Chloramphenicol
		Benzyl Alcohol
		Sulfisoxazole
		5. Breast-milk jaundice (early-onset)
		6. Metabolic disorders
		Galactosemia
		Hypothyroidism

Table-2: Maternal risk factors.

Maternal:	Mother # 1	Mother # 2
1. Ethnic group	Asian	Asian
2. Parity	0+0	3+0
3. Booked/Unbooked Pregnancy	Booked	booked
4. Complications during pregnancy: Gestational DM, Pre-eclampsia / Eclampsia, ABO incompatibility, Rh incompatibility, TORCH infections	None	none
5. Chronic conditions: DM, HTN, Epilepsy, Hepatitis B or C etc.	None	none
6. Medications used during pregnancy	Folic acid, Iron, Calcium supplements	Folic acid and iron supplements
7. Gestational age at delivery	34 weeks	36 weeks
8. Mode of delivery	Spontaneous vaginal delivery	Spontaneous vaginal delivery
9. Place of delivery	Darul-Sehat Hospital	AKUH (Stadium road)
10. History of delayed cord clamping	no	no

ABO:
TORCH: Towards a Revolution in COPD [chronic obstructive pulmonary disease] Health
DM: Diabetes mellitus
HTN: Hypertension
AKUH: Aga Khan University Hospital.

Table-3: Neonatal risk factors.

Neonatal:	Patient # 1	Patient # 2
1. Sex	Female	Male
2. Preterm / Fullterm	34 weeks	36 weeks
3. Birth weight	2.8 kg	2.66 kg
4. Blood group	B+ve	A+ve
5. Need for resuscitation?	no	no
6. Birth trauma: Cephalohematoma, Ecchymoses	no	no
7. What day of birth did the baby develop jaundice?	6th	4th
8. Peak bilirubin level	33.6 mg/dl	44.2 mg/dl
9. Peak bilirubin level at the day of life	6th	6th
10. Did the baby require:	Phototherapy: 2 days	Phototherapy: 3 days
Phototherapy: _____ days	Exchange transfusion: 1 time	Exchange transfusion: 1 time
Exchange transfusion: _____ times		
Both		
None		
11. Sepsis / Infection?	Negative	Negative
Blood Culture result		
12. Medications given after birth? Streptomycin	None	None
Chloramphenicol		
Benzyl alcohol		
Sulfisoxazole		
13. Family history of Gilbert's syndrome, Crigler-Najjar syndrome, G6PD deficiency, Pyruvate kinase deficiency, Hexokinase deficiency, Spherocytosis, Elliptocytosis	None	None
14. Haemoglobin level?	17	15.2
15. Reticulocyte count?	1.09	2.5
16. Thyroid Stimulating Hormone level?	4.55	1.08
17. G6PD level?	Not done	5.0 (deficient)
18. Hearing test results?		
1st:	Failed (13th day of life)	Failed (16th day of life)
2nd:	Not done	Failed (2 months)
19. Follow-up visit with improvement in hearing, approximate age?	8 months	1 year 5 months
20. Speech at follow-up visit?	Normal for age, talking in sentences at 2 years of age	Speaking 2-3 words and responding to commands at 1 year 5 months of age.

G6PD: Glucose-6-phosphate dehydrogenase deficiency.

normal limits and blood sulture/sensitivity (C/S) was negative. Brainstem audiometry-evoked potential (BAER) was done on 13th day of life that showed severe bilateral peripheral auditory pathway dysfunction. She was regularly followed up and improvement in hearing was first noted at 8 months of life when she started responding to verbal commands. At a follow-up visit at 1 year 3 months of age, she was able to hear fine and at 2 years, her speech was normal for age.

Our second patient was a boy born at 36 weeks of gestation by normal vaginal delivery. No complications were noted during pregnancy or delivery with Activity-Pulse-Grimace-Appearance-Respiration (APGAR) score being 8 at 1 minute and 9 at 5 minutes. Birth weight was 2.66kg. He developed unconjugated hyperbilirubinaemia on fourth day of life with peak bilirubin level reaching 44.2 mg/dl (indirect=42.4; direct=1.8) on sixth day of life. No family history of enzymatic or metabolic disorders was present. He underwent 3 days of phototherapy and 1 exchange transfusion. Lab investigations, including Hb, reticulocyte count and TSH was normal and blood C/S was negative. Glucose-6-phosphate dehydrogenase deficiency (G6PD) level was 5.0 thus showing the neonate to be G6PD-deficient. BAER done on 16th dayof life showed severe bilateral peripheral auditory pathway dysfunction. Magnetic resonance imaging (MRI) done on 16th day of life showed changes of hyperbilirubinaemia encephalopathy. Spontaneous improvement in hearing was first noted at the age of 1 year when he started speaking words and responding to verbal commands.

Discussion

Neonatal hyperbilirubinaemia, a condition characterised by an excessive concentration of bilirubin in blood, remains the most common health issue in neonatal age group. Direct

(conjugated) and indirect (unconjugated) are the two types of hyperbilirubinaemia. Jaundice is more common in neonates, primarily pre-term newborns, because of high Hbmass (18-22 mg/dl) and more than 75% of Hbbeing foetal Hbwhich is unstable at high oxygen tension and has short life span.[11] Unconjugated bilirubin accumulates due to relatively decreased rate of bilirubin conjugation by the liver. This results in deposition of unconjugated lipid-soluble bilirubin in skin and mucus membranes.[12]

Neurological concentration of unconjugated bilirubin can lead to kernicterus, which is the most serious complication of neonatal jaundice.[1] Other sequelae include bilateral choreoathetosis and other neurological disorders such as sensorineural hearing loss,[1,8] as auditory pathway is one of the most sensitive parts of the nervous system to bilirubin-induced neurotoxicity.[10,13] Hence, follow-up until school age is recommended for evaluation of extrapyramidal symptoms and auditory functions.[14]

Some spontaneous improvement in auditory dysfunction as a complication of hyperbilirubinaemia in infants has been reported. A retrospective study found spontaneous improvement in hearing loss in about 50% of infants within 15 months of diagnosis. Out of all the children with auditory neuropathy, those who had developed auditory loss as a consequence of neonatal hyperbilirubinaemia showed a greater tendency to improve spontaneously.[15]

Our patients developed unconjugated neonatal hyperbilirubinaemia that required exchange transfusion and subsequently developed early-onset sensorineural hearing loss as evidenced by the results of BAER. Prompt management with phototherapy and exchange transfusion and regular follow-up of the cases revealed spontaneous improvement in hearing loss. A study involving patients with neonatal jaundice highlighted the fact that acoustic evoked potential audiometry should be done in assessment of infants after neonatal jaundice.[16]

These cases emphasise the value of awareness among physicians regarding this condition that can help in timely detection of risk factors and prompt clinical monitoring and follow-up.

Although a final conclusion cannot be drawn from a Case Report, but from our two cases it seems re-assuring that the hearing loss may be transient, if developed after severe hyperbilirubinaemia. Large-scale studies are required to confirm our findings and to determine the appropriate course of action which should ensure that timely intervention does take place, but dramatic interventions like cochlear implantation should only be opted for after a thorough follow-up and evidence of a stable condition without spontaneous improvement.

Conclusion

Neonatal hyperbilirubinaemia may be complicated by sensorineural hearing loss as auditory pathway is one of the most sensitive parts of the nervous system to this toxic agent, but if all possible risk factors are managed promptly with a vigilant follow-up, then these hazardous complications can be avoided. Follow-up of all infants and of appropriate family counselling regarding all possible outcomes, including remission, is necessary.

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