CORELATION BETWEEN NEONATAL SEPSIS AND CHOLESTATIC JAUNDICE IN A CASE OF PREMATURE NEWBON

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Abstract

Sepsis is a major cause of morbidity and mortality in newborns, especially in premature babies due to associated immunological deficiencies and comorbidities. Although not common in medical practice, secondary cholestatic jaundice raises major problems, and the three entities - sepsis, cholestatic jaundice, prematurity - may cause or exacerbate the vicious circle of prolonged neonatal jaundice, because of difficulties in diagnosis and treatment . Thus the prognosis is often poor and the evolution of the disease with multiple complications. Case Presentation: This is the case of a premature infant with very low birth weight (VLBW) with associated pathology, who developed cholestatic jaundice. Severe neonatal sepsis and prematurity accounts for pathologies that can cause and aggravate the jaundice with immediate and remote neonatal complications. The determinants of neonatal cholestasis: infectious, obstructive, genetic, metabolic, endocrine. The intricate causes led to the complicated evolution and prolonged hospitalization. Conclusions: Gestational age must be documented for each newborn and it is an important predictor of the risk of developing hyperbilirubinemia. Neonatal sepsis associated with prolonged jaundice will complicate the evolution and TORCH pathology is difficult to be ruled out. Obstructions or anatomical malformations of bile ducts are difficult to detect by imaging methods in this group of patients, very low birth weight being an impediment to the investigation.

Key words: prematurity, sepsis, prolonged cholestatic jaundice

Introduction

Sepsis is the leading cause of neonatal mortality, despite the progress of modern medicine, having been reported annually over 6 million deaths. [1] Early-onset neonatal sepsis is caused by infections acquired through maternal-fetal transmission, and the late-onset nosocomial always. Onset is much faster in premature infants. In prematurs with VLBW, due to the need of prolonged hospitalization periods,the risk of developing late-onset sepsis is higher. [2] Identification of the risk factors and the proper use of protocols for diagnosis of neonatal sepsis with prompt and appropriate treatment, will decrease the hospitalization days and the mortality and morbidity of newborns. [3]

The risk of developing severe jaundice is inversely related to gestational age. Premature infants will have increased risk of developing bilirubin encephalopathy thus they require careful monitoring of total serum bilirubin. Cholestasis, defined as a decrease in the secretion of bile flow due to damage to the hepatocyte or bile flow obstruction with intrahepatic bile ducts extra or is caused by any condition which substances normally excreted in the bile are retained.

Case Presentation

The newborn B. M. female was hospitalized at 4 days of life in ICU of Premature Children Emergency Hospital "Louis Turcanu" in Timisoara. The newborn was born by Caesarean section in cephalic presentation at a gestational age of 32 weeks, with birth weight 1080g and IA = 5 at 1 minute. Please note that in the delivery room required positive pressure ventilation and cardiac massage.

On admission showed a serious general condition, jaundice of the skin and sclera; repeated episodes of apnea, arrhythmia and respiratory distress, with biological samples conclusive for sepsis.

Admission laboratory data confirmed the jaundice: BD = 27.57 umol / l, BT = 162.35 umol / l. She presented with changes in blood count with severe thrombocytopenia (Le = 4.470 UI, Hb = 16.2 g / dL, Ht = 47%, PLT = 1,000 IU). Inflammatory markers were elevated (CRP = 110.56 mg / L, procalcitonin = 77.37 ng / ml) with positive blood cultures for Klebsiella Pneumonia (48h).

Evolution during hospitalization was slow, with a slow upward curve weight (from 1050 to 2560g). It required O2 therapy with VM due to multiple episodes of apnea episodes and psychomotor agitation. Sclero jaundice - skin persisted throughout the period of hospitalization, with mild but never full remission episodes. In evolution the newborn developed bilious vomiting , distended abdomen, acholic stools, meteorism. Dark urine emerged late in evolution, from 76 days of life with favorable outcome.

Inflammatory samples became negative but increased CRP persisted during hospitalization under poly-broad spectrum antibiotics. (Fig. 1)

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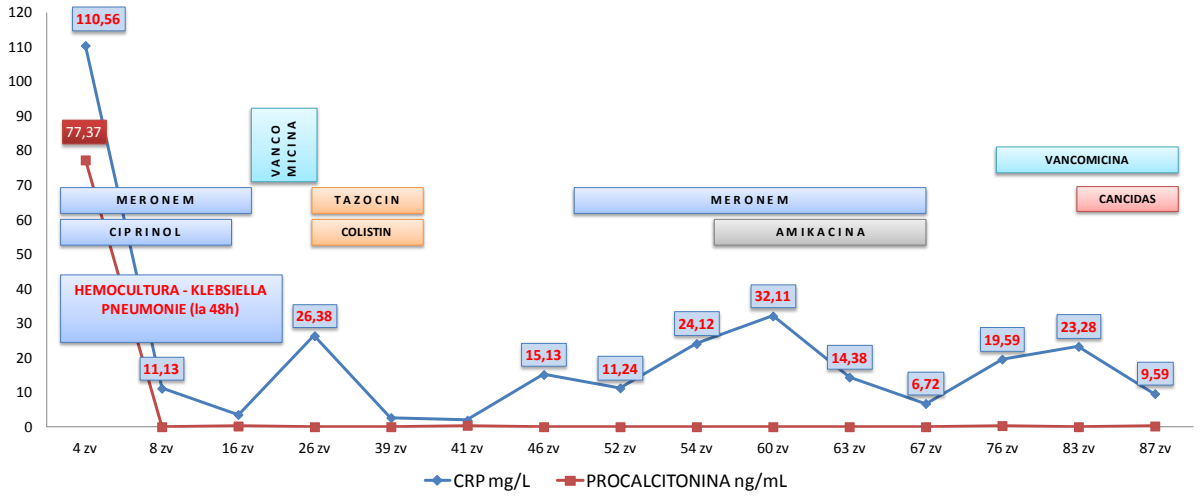

Fig. 1. Evolution of inflammatory markers, dynamics.

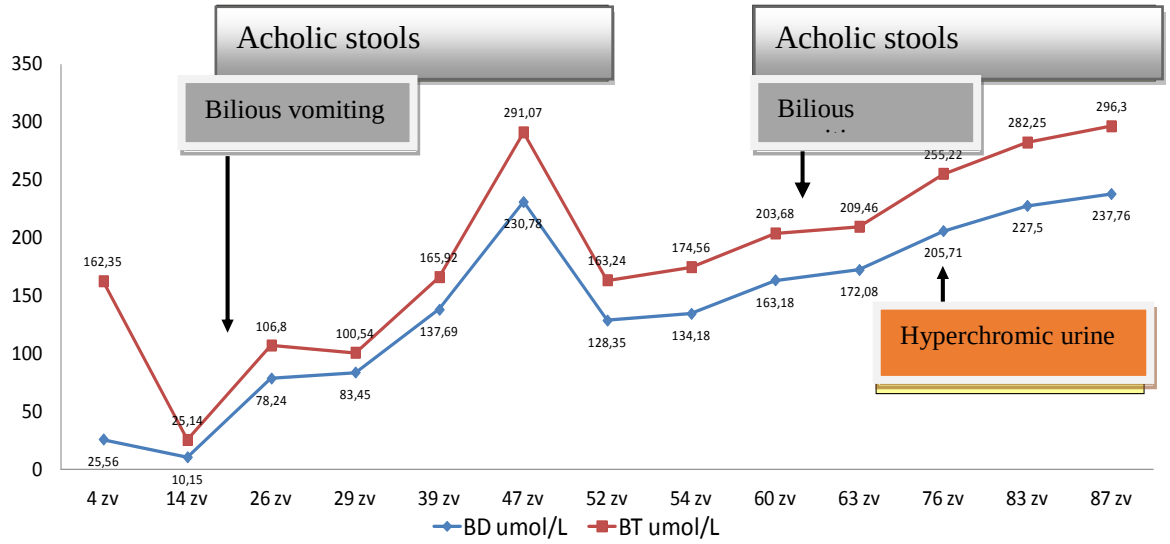

Fig. 2. Hipebilirubinemia, dynamics.

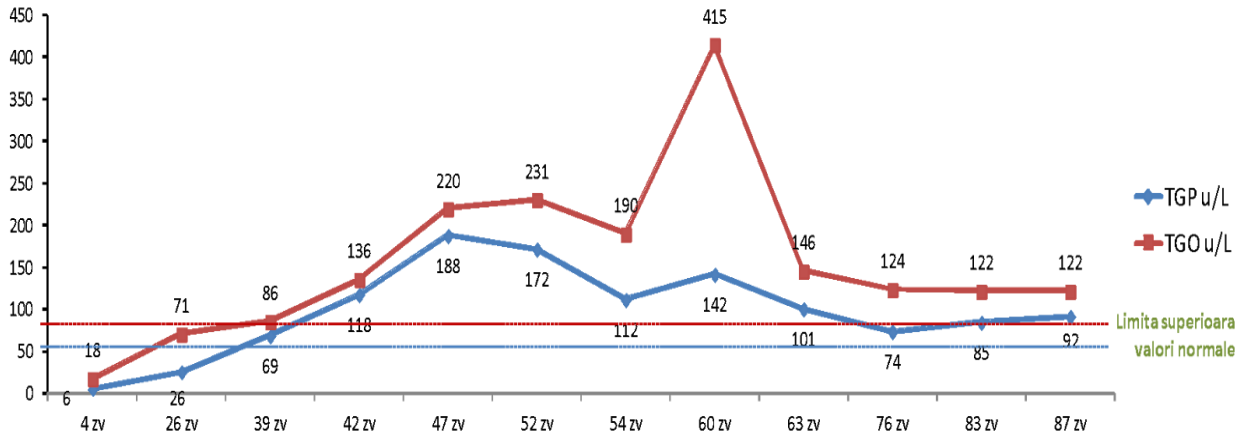

Fig. 3. Evolution of transaminases, dynamics.

Table 1. Causes of neonatal jaundice.

NEONATAL CHOLESTASIS		
Infectious		**Genetic (25%) , metabolic (20%), endocrine**
Viral	adenovirus; cytomegalovirus; coxsackievirus; Epstein-Barr; echovirus; enterovirus; hepatitis A, B, or C; herpes simplex; human immunodeficiency virus; parvovirus; rubella	Prematurity
Bacterial	urinary tract infection, sepsis, listeriosis, tuberculosis	A1AT deficiency (10%)
Parasites	toxoplasmosis, malaria, toxocariasis	Bile acid synthetic defects
Spirochete	syphilis, leptospirosis	Alagille syndrome, Crigler-Najar syndrome, Gilbert syndrome
Histoplasmosis		Hypopituitarism (septo-optic dysplasia) Hypothyroidism
Anatomic obstruction		Hereditary spherocytosis Elliptocytosis G6PD deficiency Thalassemia Vitamin K induced hemolysis
Biliary atresia (23-35%) Choledochal cyst or other congenital bile duct anomaly		Autoimmune hemolytic disease Polycythaemia Galactosemia
Congenital hepatic fibrosis Inspissated bile syndrome		ABO incompatibility Rh isoimmunization
Neonatal sclerosing cholangitis		Cystic fibrosis
Tumor/mass		Drugs / hormones (progesterone)
Increased enterohepatic circulation of bilirubin		**Other**
Pyloric stenosis Intestinal atresia Ileus		Ischemia-reperfusion injury Perinatal asphyxia Hemophagocytic lymphohistiocytosis Idiopathic neonatal hepatitis Neonatal lupus erythematosus

Adapted from [4]

Determination of total and direct bilirubin in dynamic shapes, prolonged jaundice biological picture (Fig. 2).

Initially, transaminases were within normal limits, will exceed the upper limit of normal at 42 days of life and keep it elevated throughout the hospitalization (Fig. 3).

Other biological investigations Task:

− examination stool digestion starch - absent, muscle fibers - absent, fat - absent

− ELFO: albumin = 70.4% = 2.7% α1, α2 = 9.7%, β = 10%, δ = 7.2%

− Thyroid hormones (41 zv): FT3 = 2.63 pmol / L FT4 = 14.92 pmol / L, TSH = 1.56 IU / L

− cytological examination blood smear: anisocytosis, moderate anizocromy isolated red blood cells in the target Pile (50 days old) , anisocytosis, hypochromia (69 days old)

− osmotic resistance: Initial <4.2 ‰, total <2.8 ‰

− tests hemolysis: Percentage = 3.6% hemolysis, hemolysis percentage corrected glucose = 2.3%

− Test Brever - Negative

− Toxo IgG (IU / ml): Negative

− CMV IgG (U / ml): Positive (on 2 consecutive measurements)

Imaging investigations performed for prolonged jaundice etiology and complications of prematurity with VLBW for detection:

− Echocardiogram: septal defect 3-4 mm perimembranos with both shunt shunt VS-VD and VS-AD type Gerbode, VS-AD Vmax = 4.3 m / s, P max = 77 mmHg and VS-VD Vmax = 2.3 m / and P max = 23 mmHg, foramen ovale

− ETF: intraventricular haemorrhage gr II / III. Periventricular leukomalacia average form

− Eye exam: OD / under vascularized retina, OS / ROP stage 1 in zone II. At a second consultation over 18 days ROP in remission, with favorable evolution.

− Abdominal ultrasound (34 zv): Liver - normal aspect, with the longitude = 49 mm. Normal ESR. Gallbladder - hypoechogenic content with transonic zone with a large expansion of bile duct (bile duct cyst). RS - 35/15 mm, RD - 33/25 mm, echostructure normal. Stomach distended with food content. Spleen slightly oblate - 33/25 mm. Thick bile syndrome is suspected.

− MRCP (57 zv): Liver, pancreas, spleen, kidneys, adrenal normal aspect native investigation. Gallbladder plied, relaxed. Extrahepatic biliary duct normal. Without ascites. Without lymph intra / retroperitoneal. VCI, abdominal aorta normal size.

Discussion

VLBW preterm infant developed neonatal sepsis and required parenteral nutrition.

After imaging investigations a cyst of the bile duct cyst was found. All these factors have caused and prolonged the neonatal jaundice.

Multiple causes of cholestatic jaundice in the literature are cited.

Neonatal cholestasis is characterized by an increased serum level of BD in the first 90 days. Cholestasis indicators are: BD serum levels> 17 micromol / L or 1 mg / dl, or BD serum level of> 20% of BT concentration (if BT is> 85 micromol / l or 5 mg / dl) [10] [11].

Neonatal cholestasis affects about 0.04 to 0.2% of newborns. According to the literature about 40-60% of cases of cholestasis are associated with prolonged parenteral nutrition, the rest of the etiologies cases occur due to the following:

Energy demand is of great importance. The growth deficit is secondary to failure of fat absorption, impaired metabolism of proteins and carbohydrates, as well as increased metabolic demands. Oral nutrition is the preferred route of administration. In most cases additional vitamins (K, E, D) are required. [8], [9]

Short-term prognosis is unfavorable, with evolving jaundice and low survival rate due to multiple comorbidities (neonatal sepsis, anemia mixed prematurity, infection). In the long term, according to some authors (Robertson and Howarth), permanent deafness may occur (3.1% of cases) or severe hearing loss (1.9% of cases) if VLBW preterm [5]. Extension brain damage and retinopathy of prematurity may predict risk of severe disability at age 11 major. [6] proinflammatory molecules due to sepsis may have a negative effect on neurological development with cognitive impairment and cerebral palsy. [7]

Prognosis is worsened by hepatic impairment due to the evolution of liver cell destruction , low weight due to prematurity and disease, intraventricular hemorrhage and periventricular leukomalacia evolving toward psychomotor retardation.

Conclusions

VLBW preterm represent an impediment to the necessary investigations to establish the etiology, low birth weight is a morbid entity (the major factor increasing bilirubin).

Gestational age is a major predictor of risk of developing hyperbilirubinemia (jaundice extended) and should be evaluated and documented for each newborn.

The combination of multiple factors: early neonatal sepsis, prematurity, prolonged partial parenteral nutrition had a major role in the persistence of cholestatic jaundice.

Imaging studies are useful to detect gallstones or biliary malformations intra or extrahepatic. This may use ultrasound and endoscopic retrograde cholangiography MRCP with contrast material.

Velasco Cerrudo (16) tries in 1992 a score of practical use.

References

1. Kissoon N, Carcillo JA, Espinosa V, Argent A, Devictor D, Madden M, Singhi S, van der Voort E, Latour J. World Federation of Pediatric Intensive Care and Critical Care Societies: Global Sepsis Initiative. Pediatr Crit Care Med, 2011. 12(5): p. 494-503.
2. John P. Cloherty, Eric C. Eichenwald, Anne R. Hansen, Ann R. Stark Manual of Neonatal Care, seventh edition, p624
3. Larsen GY, Mecham N, Greenberg R. An emergency department septic shock protocol and care guideline for children initiated at triage. Pediatrics. Jun 2011;127(6):e1585-92.
4. Amy G. Feldman, MD, Ronald J. Sokol, MD - Neonatal Cholestasis, NeoReviews Vol.14 No.2 February 2013 e63-73)
5. Robertson CM, Howarth TM, Bork DL, Dinu IA. Permanent bilateral sensory and neural hearing loss of children after neonatal intensive care because of extreme prematurity: a thirty-year study. Pediatrics. May 2009;123(5):e797-807.
6. Farooqi A, Hägglöf B, Sedin G, Serenius F. Impact at age 11 years of major neonatal morbidities in children born extremely preterm. Pediatrics. May 2011;127(5):e1247-57.

7. Adams-Chapman I, Stoll BJ. Neonatal infection and long-term neurodevelopmental outcome in the preterm infant. Curr Opin Infect Dis. Jun 2006;19(3):290-7.
8. Javid PJ, Malone FR, Dick AA, et al. A contemporary analysis of parenteral nutrition-associated liver disease in surgical infants. J Pediatr Surg. 2011;46(10):1913–1917
9. Rangel SJ, Calkins CM, Cowles RA, et al; 2011 American Pediatric Surgical Association Outcomes and Clinical Trials Committee. Parenteral nutrition-associated cholestasis: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. J Pediatr Surg. 2012;47(1):225–240
10. Linn S, Schoenbaum SC, Monson RR, Rosner B, Stubblefield PG, Ryan KJ. Epidemiology of neonatal hyperbilirubinemia. Pediatrics. Apr 1985;75(4):770-4
11. Allen K, Whitington PF – Evaluation of liver function in Polin R, Fox W: Fetal and Neonatal Physiology, Philadelphia, ed 2, WB Saunders, 1995.

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