

# Two cases of neonatal adrenal hemorrhage presenting with persistent jaundice

*Due casi di emorragia surrenalica neonatale manifestatasi con ittero persistente*

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## Abstract

The adrenal hemorrhage is a relatively rare event in newborns but must be considered in the presence of a persistent unexplained jaundice, especially in presence of predisposing factors. Serial ultrasonography is the modality of choice for initial diagnosis and follow-up of neonatal adrenal hemorrhage.

We report two cases of neonatal adrenal hemorrhage presenting with persistent jaundice. The causes of the neonatal adrenal hemorrhages were a difficult vaginal delivery in macrosomic infant and a neonatal infection.

## Riassunto

L'emorragia surrenalica è un evento relativamente raro nei neonati ma deve essere considerata in presenza di ittero persistente inspiegabile, specialmente in presenza di fattori predisponenti. L'esame ecografico seriato è la modalità di prima scelta per la diagnosi iniziale e il follow-up dei neonati con emorragia surrenalica. Riportiamo due casi di emorragia surrenalica neonatale manifestatesi con ittero persistente. Le cause correlate ai due casi di emorragia surrenalica presentati erano un parto vaginale difficile di un neonato macrosoma e un' infezione neonatale.

## Introduction

Adrenal hemorrhage (AH) is unusual in infants and occurs most often after a traumatic delivery or a complicated neonatal course. The most common clinical symptoms are abdominal mass, jaundice and mild anemia. Persistent neonatal jaundice is rarely the primary presentation.<sup>1</sup> The finding of an adrenal mass may lead to problems of differential diagnosis with other serious illnesses such as cystic neuroblastoma.<sup>2</sup> We report two cases of neonatal AH confirmed by abdominal ultrasonography (US) and magnetic resonance imaging (MRI) presenting with persistent jaundice. The causes of neonatal AH were a difficult vaginal delivery in a macrosomic infant and a neonatal infection.

## Case Report

### Case 1

A two-day-old male infant was transferred to our hospital with a fever, elevated CRP and thrombocytopenia. In another medical center, the child was born by normal spontaneous vaginal delivery at 39+1 weeks of gestation after an uneventful pregnancy. Birth weight was 4100 g and APGAR scores were 8 and 10 at 1 and 5 minutes, respectively.

Systemic examination was normal except for icterus and irritability. Laboratory results confirmed the increase of CRP (10 mg/dl) and thrombocytopenia ( $91 \times 10^6 /l$ ) with normal coagulation parameters and blood chemistry.

Therapy was started with Ampicillin and Gentamycin. At three days of life, high values of serum bilirubin (15,3 mg/dl) with direct fraction of 0,9 mg/dl phototherapy was started. Within a few days the CRP and platelet levels normalized, while blood and CSF cultures were negative. Antibiotic therapy was discontinued after 10 days. At 15 days of life, elevated total serum bilirubin (18,4 mg/dl) with direct bilirubin 0.6 mg/dl persisted. The infant was fed formula milk. Both baby and mother had A+ blood group and Coombs test was negative. Laboratory studies revealed hemo-

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globin of 13,5 g/dl, reticulocyte count of 1,5% and liver function tests were normal. Urine analysis and culture were normal and the urine tested negative for reducing substances. Serum glucose-6-phosphate dehydrogenase and thyroid concentrations were all normal. The Cranial ultrasonography (US) was normal but abdominal US revealed a heterogeneous soft-tissue mass lesion consistent with an adrenal hematoma 35 mm right and 29 mm to the left. Magnetic resonance imaging (MRI) of the abdomen confirmed the picture without enhancement and/or calcifications. 24-hour urinary vanillylmandelic acid/catecholamine levels were normal. Serial ultrasound examinations showed significant reduction of AH. At 20 weeks of life, abdominal US showed slight increase in volume of the adrenal gland, in particular on the right, but no structural alterations.

### Case 2

A nineteen-day-old female infant, fed formula milk, was admitted to our hospital for jaundice. The child was born at 41+2 weeks gestation to a 36-year old woman after an uneventful pregnancy. A difficult vaginal delivery, carried out without instrumental assistance, led to a fracture of the infant's right clavicle. Birth weight was 5150 g and APGAR scores were 9 and 10, at 1 and 5 minutes, respectively. She was discharged on fourth day with total serum bilirubin 12,6 mg/dl.

The infant's weight was 5210 g and systemic examination was normal except for icterus and a hard lump on the right clavicle. Laboratory studies revealed: total serum bilirubin of 18,6 mg/dl; direct bilirubin of 0,5 mg/dl; hemoglobin: 14,8 g/dl; reticulocyte count of 2%; and liver function tests were normal. Both baby and mother had 0+ blood group and infant was Coombs negative. Urine analysis and culture were normal and the urine tested negative for reducing substances. Serum glucose-6-phosphate dehydrogenase and thyroid concentrations were all normal.

Cranial US was normal but abdominal US revealed an oval mass of 42 mm, a prevalently solid structure of the right adrenal gland. This picture was confirmed by abdominal MRI. There was no enhancement in the post-contrast or calcification in the mass (figure 1). Coagulogram and 24-hour urinary vanillylmandelic acid/catecholamine levels were normal. Serial ultrasound examinations showed significant reduction of AH (figure 2). At 16 weeks old, the abdominal US was normal.

### Discussion

Persistent jaundice in the neonate is defined as jaundice that lasts longer than 14 days; it can occur in up to 15% of all newborns. The vast majority of these neonates have unconjugated hyperbilirubinaemia and the most known causes include breast milk jaundice, haemolytic diseases, galactosemia, hypothyroidism, urinary tract infection and blood extravasation.<sup>3</sup>

The main guidelines for the management of an infant with persistent jaundice are reported among the most common forms of blood

extravasation, cephalohematoma and significant bruising. There is no data pertaining to other sites where internal hematomas may occur such as spleen, liver, internal cranium and adrenal glands.<sup>4</sup> Although AH is an unusual event in newborns, it may present with persistent jaundice.<sup>1</sup>

AH usually occurs at birth or during the immediate postnatal period and the incidence ranges from approximately 1.7 to 2.1 per 1000 births. It affects the right side more than the left side and is bilateral in 10 to 15% of the cases. In the newborn, the adrenal gland is very large compared to weight and unique vascular supply; for this reason it is more vulnerable to vascular damage. Any condition leading to hypoxia may lead to shunting of blood flow to vital organs. The increased pressure associated with congestion and the damaged endothelial cells associated with hypoxia may cause AH.<sup>1</sup> Birth trauma, prolonged labor, intrauterine infection, perinatal asphyxia or hypoxia, large birth weight, septicemia, hemorrhagic disorder and hypochrominemia are the most common predisposing factors of AH.<sup>1</sup>

Clinical manifestations of adrenal hemorrhage can vary depending on the degree and rate of hemorrhage, as well as the amount of adrenal cortex compromised by the hemorrhage. Although an isolated focal unilateral AH may present subclinically, massive bilateral AH may present in shock. Large unilateral or bilateral extensive bleeds may also present with palpable flank mass, mild anemia, jaundice or scrotal hematoma.<sup>5,6</sup> Addisonian crisis is rare in AH because hemorrhage is predominantly subcapsular and adrenal insufficiency does not occur until at least 90% of adrenal tissue is destroyed.<sup>7</sup>

Neonatal jaundice is common and occurs due to hemolysis from enclosed hemorrhage. Persistent neonatal jaundice is rarely the primary presentation.<sup>8,9</sup>

The finding of an adrenal mass may lead to serious problems of differential diagnosis as other serious pathological entities such as cystic neuroblastoma must be considered.<sup>2,10</sup>

Postnatal diagnosis of cystic neuroblastoma may be obtained by indirect signs such as collection of 24-h urine specimen to measure vanillylmandelic acid, and by radiological examinations such as US or MRI.<sup>2,11</sup> Although the imaging results of two groups of cystic lesions were similar, the failure of prenatal detection, the absence of calcification on initial images, and the size reduction are all factors that suggest AH.<sup>12,13</sup> For these reasons, serial US is the best modality for monitoring AH to prevent unnecessary surgery.<sup>14</sup>

In our patient VMA levels were normal; there was no calcification, and follow-up US revealed decrease in size of the cyst.

### Conclusion

The possibility of AH as a cause of persistent jaundice should not be ignored, especially in children with predisposing factors. In addition, the importance of a correct differential diagnosis with cystic neuroblastoma through a follow-up US is emphasized.

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