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Hemoperitoneum and disseminated intravascular coagulation in two neonates with congenital bilateral neuroblastoma

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Abstract We report two neonates with anemia, hemoperitoneum, and bilateral palpable abdominal masses. Both developed bleeding: a hemoperitoneum in one and visceral hemorrhages secondary to disseminated intravascular coagulation in the other. Each child was thought to have an unusual complication of adrenal hemorrhage, as the masses were of mixed echogenicity. However, histological evaluation revealed neuroblastoma. These cases point out the diagnostic dilemma of a mixed echogenicity suprarenal mass in the neonatal period and emphasize that local and disseminated bleeding can occur as a major manifestation of neuroblastoma.

Introduction

Congenital neuroblastoma is the most common neonatal malignancy with 93% located in the adrenal gland [1]. The lesion may be solid (56%) or cystic (44%) [2]. While hemorrhage is a recognized complication of congenital neuroblastoma, neonatal hemoperitoneum as a sequela is rare. Separating cystic neuroblastoma and adrenal hemorrhage remains a diagnostic dilemma, as the sonographic characteristics may be identical. Other imaging modalities including color flow Doppler, CT and MR provide little help in resolving this diagnostic difficulty. We present two neonates with anemia and bilateral suprarenal masses. One developed hemoperitoneum and the other visceral hemorrhages secondary to disseminated intravascular coagulation (DIC). In both cases the masses were congenital neuroblastoma.

Case report

Case 1

A 2,868 g male was born at 38 weeks' gestation. The pregnancy was complicated by marijuana abuse, high blood pressure, and premature labor. The intrapartum events included passage of meconium. Apgar scores were 8 at 1 min and 9 at 5 min.

The baby had mild respiratory distress requiring hood oxygen. On the second day he was noted to have a left upper quadrant/flank mass. His hematocrit fell from 46% to 26% and platelets dropped from 191,000 to 71,000. The prothrombin (PT) was 15.5 s (normal range 10.6–13.1 s) and activated partial thromboplastin time (PTT) was 39.5 s (normal range 19.5–31.1 s). Vanillylmandelic acid and homovanillic acid levels were not elevated. The physical examination revealed a quiet, pink, term infant in no distress. The abdomen was distended with a palpable mass.

Ultrasound of the abdomen on the second day of life showed a rounded 4.8 × 4.4 × 5.4 cm, mixed echogenic left flank mass. It flattened and displaced the left kidney inferiorly (Fig. 1). Minimal, if any, color flow was seen within the adrenal mass. No calcification was noted. These findings were thought to be consistent with adrenal hemorrhage. The right adrenal gland was prominent and hypoechoic. Pelvic fluid was thought to be secondary to intraperitoneal hemorrhage. Exploratory laparotomy was performed to control blood loss, and the mass was resected with a histologic diagnosis of neuroblastoma (Fig. 1).

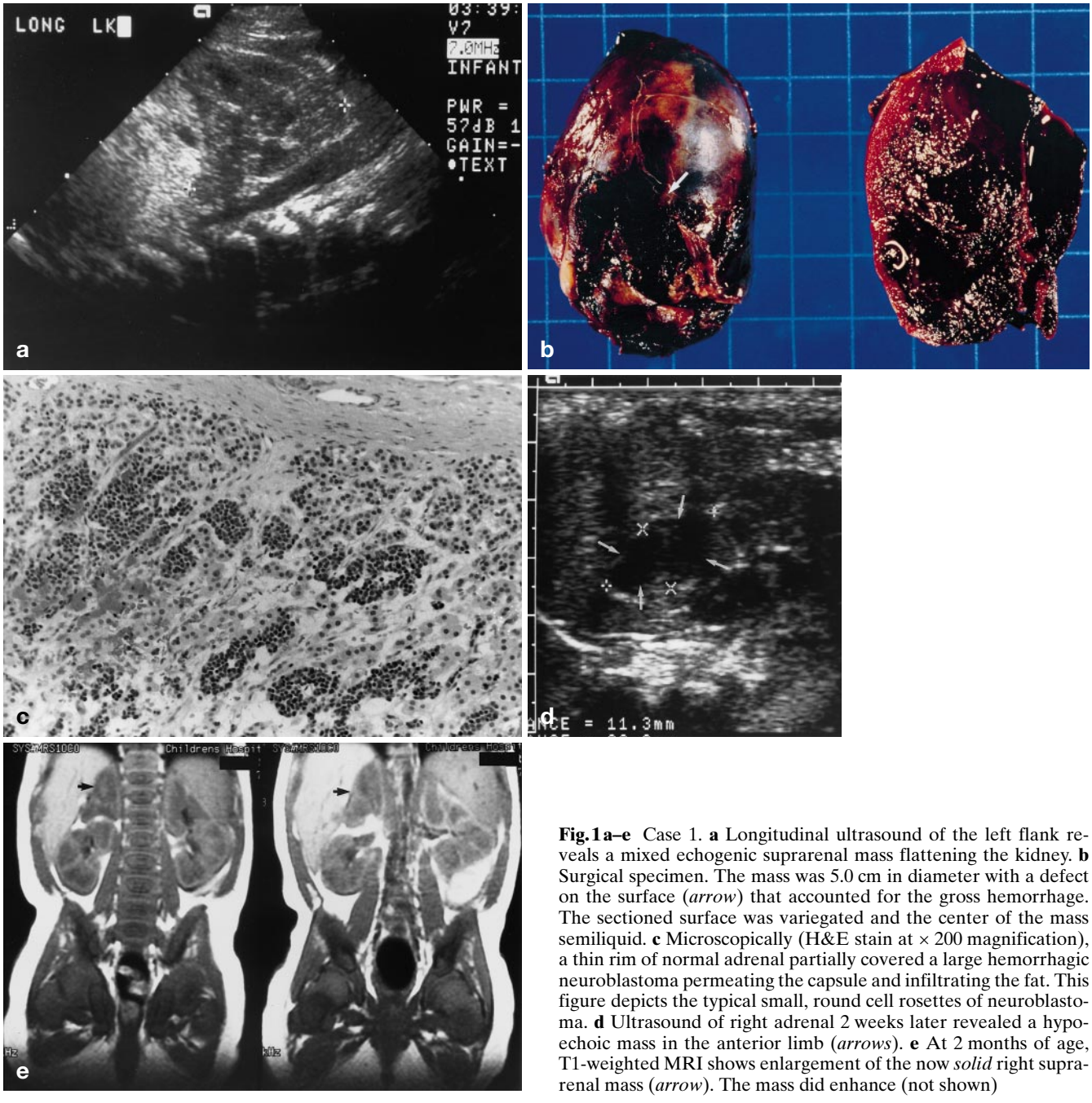

Fig. 1 a–e Case 1. **a** Longitudinal ultrasound of the left flank reveals a mixed echogenic suprarenal mass flattening the kidney. **b** Surgical specimen. The mass was 5.0 cm in diameter with a defect on the surface (*arrow*) that accounted for the gross hemorrhage. The sectioned surface was variegated and the center of the mass semiliquid. **c** Microscopically (H&E stain at × 200 magnification), a thin rim of normal adrenal partially covered a large hemorrhagic neuroblastoma permeating the capsule and infiltrating the fat. This figure depicts the typical small, round cell rosettes of neuroblastoma. **d** Ultrasound of right adrenal 2 weeks later revealed a hypoechoic mass in the anterior limb (*arrows*). **e** At 2 months of age, T1-weighted MRI shows enlargement of the now *solid* right suprarenal mass (*arrow*). The mass did enhance (not shown)

Ultrasound 2 weeks later showed a hypoechoic mass in the anterior limb of the right adrenal – a change from the first ultrasound (Fig. 1). Four weeks after operation, repeat ultrasound of the abdomen showed a *solid* mass flattening the superior pole of the right kidney. MR revealed high signal on T2, low signal on T1, and marked contrast enhancement of the enlarged right adrenal gland (Fig. 1). Bone scan showed no evidence of metastasis. The presumed diagnosis of a second neuroblastoma was made.

The patient received chemotherapy (Cytoxin, Adriamycin), and the CT scan 1 month later showed resolution of the right suprarenal mass. At no time were tumor markers elevated. He is alive and disease free at age 3 years.

Case 2

A 3,300 g baby girl was born at term. The vaginal delivery was complicated by meconium aspiration. Apgar scores were 5 and 9. She was tachypneic with a distended abdomen and palpable abdominal masses. Her abdominal girth rapidly increased, and she

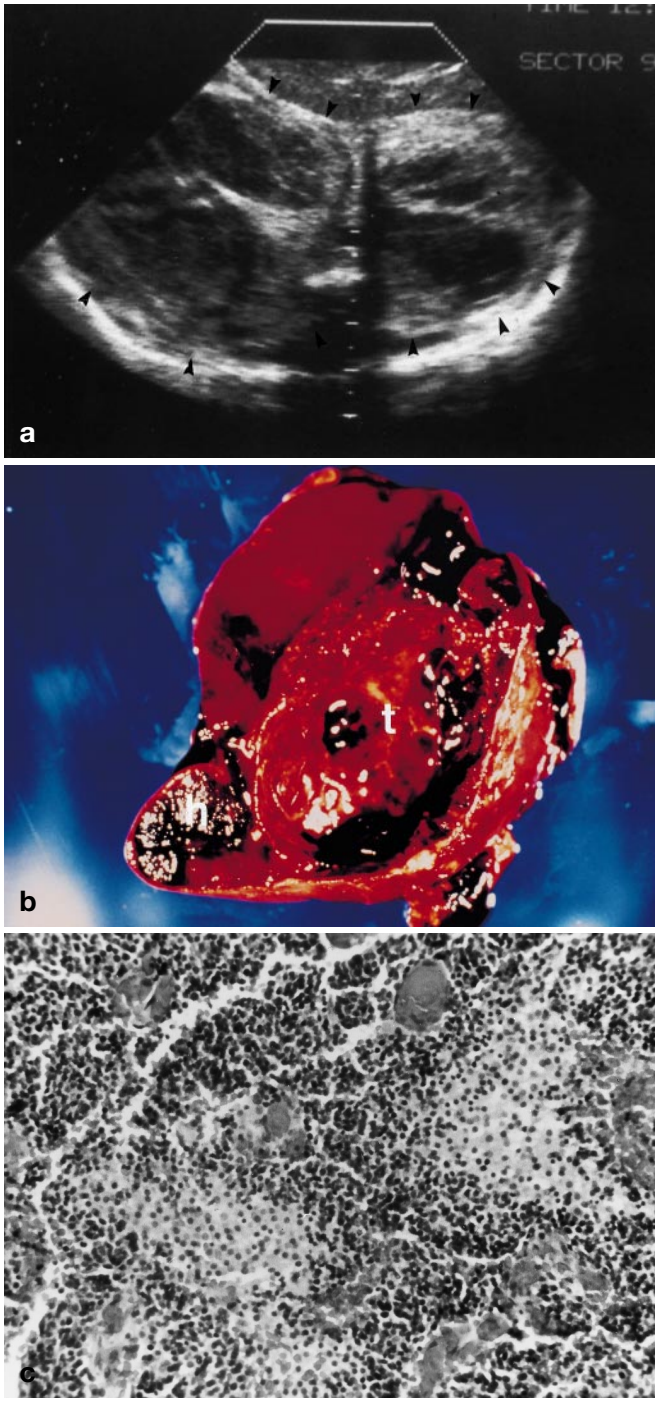

Fig. 2 a–c Case 2. **a** Supine transverse sonogram shows bilateral mixed echogenic adrenal mass (*arrowheads*). **b** The adrenals at autopsy were inhomogeneous with areas of hemorrhage (*h*), solid tumor (*t*). The cyst area is not shown. **c** Histologic examination (H&E stain with × 400 magnification) showed neuroblastoma characterized by collections of small regular cells sometimes forming nests surrounding pink fibrillary material. Extensive hemorrhage and necrosis with areas of calcification were noted

developed bleeding from respiratory, gastrointestinal, and urinary tracts. Transverse, supine, abdominal ultrasound showed bilateral suprarenal masses of mixed echogenicity filling the abdomen (Fig. 2). PT was 35.1 (normal 10.8–13.8), PTT was 120 (normal 23–42), fibrinogen was 29 mg/dl (normal 182–367), platelets were 9,000, and fibrin split products were 1536 μm/ml (normal 0–10). The baby had disseminated intravascular coagulation, remained acidotic, anuric, hypoxic and became bradycardic, and died.

Autopsy findings revealed congenital bilateral adrenal neuroblastoma with hemorrhage and necrosis, hemorrhagic pneumonia, "shock" lung, multiple visceral hemorrhages, and choroid plexus hemorrhage. The most immediate cause of death was respiratory failure secondary to the "shock" lung. Evidence of DIC at autopsy included fibrin thrombi and multiple focal hemorrhages within the viscera. The adrenal glands were filled with hemorrhagic material (Fig. 2). Focal areas of calcification in the cyst wall were noted bilaterally. Histologic examination showed neuroblastoma characterized by collections of small regular cells sometimes forming nests surrounding pink fibrillary material. Extensive hemorrhage and necrosis with areas of calcification were noted (Fig. 2).

Discussion

Adrenal neuroblastoma and adrenal hemorrhage are being increasingly diagnosed in utero as the use of sonographic screening has increased [1–12]. Neuroblastoma is the most common neonatal malignancy and the adrenal gland the most common primary site [1, 7].

Atkinson et al. [11] and Tubergen and Heyn [13] described neonates with an adrenal mass that was a large adrenal cyst and associated neuroblastoma. The hypothesis of microcysts with neuroblastoma leading to macrocysts with neuroblastoma has not been proven [11].

Differentiation of cystic neuroblastoma from adrenal hemorrhage may be difficult. A neonatal adrenal hemorrhage associated with neuroblastoma has also been reported [14, 15]. Color Doppler has been reported to show increased flow in neuroblastoma, but was not helpful in our first patient [16, 17]. Because of the many similarities in presentation, the combined lesion must always be considered.

Differentiation of adrenal hemorrhage from neuroblastoma is generally accomplished by close follow-up with serial sonography. As opposed to neuroblastoma, adrenal hemorrhage will demonstrate changes in echogenicity and decreasing size on follow-up sonograms. Correlation with urinary homovanillic acid and vanillylmandelic acid may be helpful in excluding the presence of solid neuroblastoma, but most cystic neuroblastomas are nonfunctioning tumors [2]. Hemorrhage into neuroblastoma may cause a temporary fall in the catecholamine output of the tumor.

Neonatal adrenal hemorrhage has been reported as an unusual cause of hemoperitoneum. Although hemorrhage is a recognized complication of neuroblastoma, it is rare to find it as a cause of neonatal hemoperitoneum

[15]. Murthy et al. [15] have noted occurrence of hemorrhage in three of their six cases of neonatal adrenal neuroblastoma. In one case, the hemorrhage was confined to the gland, in another it was periglandular as well as intraglandular, and in the third it had ruptured into the peritoneal cavity.

Another rare complication of congenital neuroblastoma is disseminated intravascular coagulation. Thompson and Bosley [18] have reported a single case and found two recorded cases in the literature. The infants were very young (3 days, 10 weeks, and 3 months) and had stage 4S disease with metastases to the liver, bone marrow, and the other adrenal gland. DIC was thought to be secondary to thromboplastin release from the tumor.

In conclusion, the possibility of neuroblastoma should always be considered whenever there are hemorrhagic complications in a neonate with a cystic or mixed echogenicity suprarenal mass.

References

1. Rubenstein SC, Benacerraf BR, Retik AB, et al (1995) Fetal suprarenal masses: sonographic appearance and differential diagnosis. Ultrasound Obstet Gynecol 5: 164–167
2. Acharya S, Jayabose S, Kogan SJ, et al (1997) Prenatally diagnosed neuroblastoma. Cancer 80: 304–310
3. Lynn AAA, Parr SI, Morgan MA, et al (1997) Disseminated congenital neuroblastoma involving the placenta. Arch Pathol Lab Med 121: 741–744
4. Curtis MR, Mooney DP, Vaccaro TJ, et al (1997) Prenatal ultrasound characterization of the suprarenal mass: distinction between neuroblastoma and subdiaphragmatic extralobar pulmonary sequestration. J Ultrasound Med 16: 75–83
5. Ho PTC, Estroff JA, Kozakewich H, et al (1993) Prenatal detection of neuroblastoma: a ten-year experience from the Dana-Farber Cancer Institute and Children's Hospital. Pediatrics 92: 358–364
6. Felc Z (1995) Ultrasound in screening for neonatal adrenal hemorrhage. Am J Perinatol 12: 363–366
7. Rahman S. Ohlsson A, Fong KW, et al (1997) Fetal adrenal hemorrhage in a diamniotic, dichorionic twin: case report and review of controversies in diagnosis and management. J Ultrasound Med 16: 297–300
8. Hamada Y, Ikebukuro K, Sato M, et al (1999) Prenatally diagnosed cystic neuroblastoma. Pediatr Surg Int 15: 71–74
9. Richards ML, Gundersen AE, Williams MS (1995) Cystic neuroblastoma of infancy. J Pediatr Surg 30: 1354–1357
10. Cassady C, Winters WD (1997) Bilateral cystic neuroblastoma: imaging features and differential diagnoses. Pediatr Radiol 27: 758–759
11. Atkinson GO Jr, Zaatari GS, Lorenzo RL, et al (1986) Cystic neuroblastoma in infants: radiographic and pathologic features. AJR 146: 113–117
12. Forman HP, Leonidas JC, Berdon WE, et al (1990) Congenital neuroblastoma: evaluation with multimodality imaging. Radiology 175: 365–368
13. Tubergen DG, Heyn RM (1970) In situ neuroblastoma associated with an adrenal cyst. J Pediatr 76: 451–453
14. Eklof O, Mortensson W, Sandstedt B (1986) Suprarenal haematoma versus neuroblastoma complicated by hemorrhage. Acta Radiol Diagn 27: 3–10
15. Murthy TV, Irving IM, Lister J (1978) Massive adrenal hemorrhage in neonatal neuroblastoma. J Pediatr Surg 13: 31–34
16. Goldstein I, Gomez K, Copel JA (1994) The real-time and color Doppler appearance of adrenal neuroblastoma in a third-trimester fetus. Obstet Gynecol 83: 854–855
17. Deeg KH, Bettendorf U, Hofmann V (1998) Differential diagnosis of neonatal adrenal hemorrhage and congenital neuroblastoma by color-coded Doppler sonography and power Doppler sonography. Eur J Pediatr 157: 294–297
18. Thompson EN, Bosley A (1979) Disseminated intravascular coagulation in association with congenital neuroblastoma Postgrad Med J 55: 814–817