Case Report

Congenital Bilateral Neuroblastoma Presenting with Hepatic Failure

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Abstract: *We report a case of male neonate with anemia, abdominal mass, hemorrhagic complications, disseminated intravascular coagulation (DIC) and hepatic failure. Sonography of whole abdomen showed solid bilateral suprarenal masses. He died from uncontrolled bleedings, hepatic failure and renal failure. His autopsy revealed bilateral abdominal neuroblastoma with metastases to liver, lungs, thymus, lymph nodes but no bone marrow involvement. Congenital bilateral neuroblastoma stage IV was diagnosed. This disease is quite rare. The possibility of neuroblastoma should be considered when there are hemorrhagic complications and hepatic failure in neonate with solid echogenic suprarenal mass.*

Key Words : ● *Congenital neuroblastoma* ● *Hepatic failure*

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Neuroblastoma is one of the most common malignant tumor of infancy with 93% of cases arising in the adrenal glands.[1] About 10% of cases were involved bilateral adrenal involvement.[2,3] Congenital neuroblastoma is uncommon and about 80 cases have been reported.[4-10] Although intratumoral hemorrhage is common in neuroblastoma but massive symptomatic hemorrhage is rare.[3] We reported a male neonate with anemia, hepatic failure and bilateral suprarenal masses. He developed hemoperitoneum secondary to disseminated intravascular coagulation (DIC). Congenital bilateral neuroblastoma was diagnosed in this patient.

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Case report

A Thai male infant with uncertain gestational age was borned by normal vaginal delivery. His prenatal history was uncomplicated except materanal anemia. His mother was 17 years old and came to Siriraj Hospital due to

labor pain with no leakage. Her hematocrit on admission was 27%. Fetal ultrasound assessment revealed 39 weeks of gestational age, cardiomegaly and mass at left kidney 4x4 cm. in size. The mass was mixed solid and cystic in component. His body weight was 2,790 gm., length was 48 cm. and Ballard's score was 38 weeks. APGAR scores was 9, 10 at 1 and 5 minutes after birth. He had tachypnea, tachycardia, respiratory distress, markedly pale,and need oxygen support since birth. His abdomen was distended with hepatosplenomegaly. Other physical examination was unremarkable. Two hours after birth, he was intubated and transfered to neonatal intensive care unit (NICU) because of progressive respiratory distress.

His laboratory studies at the age of 4 hours were as followings. CBC showed Hb 10.6 g/dL, Hct 31.6%, WBC 22,900/mm^3 (Seg 35%, L 64%, Mono 1%) platelet 248,000/mm^3, NRC 5/100 WBC, MCV 95.5 fl, MCH 32.1 pg, MCHC 33.4 g/dL and RDW 18.5%. RBC morphology showed polychromasia 1+, anisocytosis 2+ and few poikilocytosis. His blood group was B, Rh positive which was the same as his mother. Direct and indirect Coomb's tests were negative. Urine examination revealed sp.gr. 1.020, pH 6, protein 4+, sugar negative, WBC 5-10/HPF, RBC 10-20/HPF. Renal function, blood chemistry and liver function test showed BUN 16 mg%, Cr 1.6 mg%, Na 149 mEq/L, K 7 mEq/L, Cl 117 mEq/L, HCO_3 4 mEq/L, glucose 91 mg%, alkaline phosphatase 137 U/L, SGOT 4,353 U/L, SGPT 2,490 U/L, GGT 312 U/L, albumin 3.4 g/dL, globulin 1.6 g/dL, total bilirubin 1.8 mg% and direct bilirubin 0.5 mg%. Coagulation studies revealed aPTT 53.5 sec (control 21-38 sec), PT 94.2 sec (control 9-14 sec), fibrinogen 86.8 mg/dL (200-400 mg/dL) and D-dimer 20,000 mcg/L (<500 mcg/L)

Tumor markers (at 2 days of age) were alpha-fetoprotein 19,641 IU/mL (normal for age), neurone specific enolase (NSE) 837 ng/mL (0-15.2 ng/mL), Beta-HCG 61.26 mIU/mL (0-3.0 mIU/mL), LDH 3,156 U/L (225-450 U/L) and ferritin 1,467 ng/mL (20-400 ng/mL).

Ultrasound whole abdomen showed hepatosplenomegaly without space occupying lesion and bilateral solid suprarenal masses approximate 4 cms. in size. Bone marrow aspiration was performed and showed hypercellularity with erythroid hyperplasia and no metastatic tumor cells.

Hospital courses: After he was intubated and supported by ventilator, broad spectrum antibiotics were given because sepsis can not be excluded. At 16 hour of age, he had progressive anemia and hypotension due to frank hematemesis. Packed red cell and fresh frozen plasma were transfused periodically but the symptoms were not resolved. Vitamin K1 was also administrated but bleeding and prolong coagulogram were not improved. The diagnosis of disseminated intravascular coagulation (DIC) was made from the prolong coagulogram, low fibrinogen and high D-dimer. Total blood exchange with fresh whole blood 1 time of his blood volume was performed for 3 cycles in 3

days in order to correct bleeding from DIC. The hematemesis was improved but he still had progressive pallor, abdominal distension and intractable hypotension. He was treated with volume expander, packed red cell, fresh frozen plasma, platelet concentrates and inotropic drugs included dopamine, dobutamin and adrenalin. Hydrocortisone was given 5 times to cortisol production rate due to suspected of adrenal insufficiency but his condition was still worsening. We planed to perform the computerized tomography (CT) of whole abdomen for finding the definite diagnosis of abdominal tumor and evaluating extension of bleeding in the abdomen but his vital signs were not stable enough to move him to radiology unit. His clinical course was complicated with renal and hepatic failure. He had progressive jaundice, impaired liver function test and decreased urine output. At 11 days of age, he developed bleeding per endotrachial tube, turned cyanosis and had bradycardia, we tried to support him with blood component and inotropic drugs but his clinical status was still worsen. He developed cardiac arrest. Cardiopulmonary resuscitation was performed but unsuccessful. Our patient was expired at 11 days of age.

The autopsy was performed and revealed bilateral congenital adrenal neuroblastoma (fig. 1), poorly differentiated subtype with metastasis to lungs, liver, thymus and lymph nodes. (fig. 2) No metastatic neuroblastoma was found in the bone marrow. The tumor cells were positive stainings for NSE and synapto-physin which confirmed the diagnosis of neuroblastoma. (fig. 3)

Fig. 1 Showed adrenal neuroblastoma

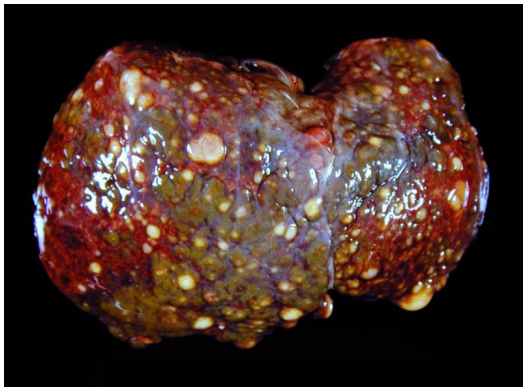

Fig. 2 Showed neuroblastoma with liver metastasis

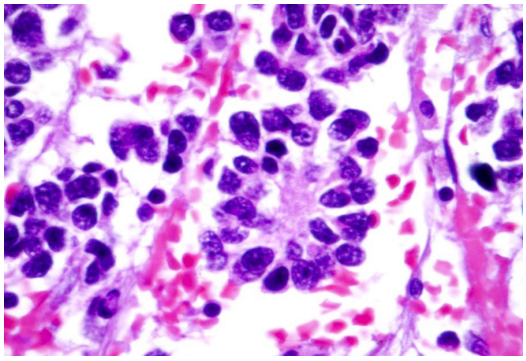

Fig. 3 Showed microscopic of neuroblastoma revealed pseudorosette formation

Discussion

Neuroblastoma is the most common solid abdominal tumor in infancy. The incidence in United states is 1 per 10,000 to 1 per 100,000 live birth.[11] Congenital bilateral neuroblastoma is quite rare. The common presentations are palpable abdominal mass, abdominal pain, fever and bone pain. Less common presentations are myoclonus, opsoclonus, cerebellar ataxia, orbital ecchymosis and intractable diarrhea. Intramural hemorrhage is common but massive symptomatic hemorrhage is rare.[3] A case of massive hemoperitoneum due to rupture of a hemorrhagic neuroblastoma has been reported.[3] Our case showed a unique manifestation of acute massive hemorrhage from tumor secondary to DIC and its hepatic metastasis, along with rapid worsening of anemia. Neuroblastoma can metastasize in utero. When present, as in our case, the fetal liver is the most common site. Most of the cases were nearly total occupied the liver parenchyma. Other sites of metastasis include the placenta, retroperitoneum nodes, paraspinal region, bone, skin and umbilical cord.[2,7,9-10,12] In this case, the autopsy revealed bilateral congenital abdominal neuroblastoma stage IV with liver, thymus gland, lymph nodes and lungs metastasis with no bone marrow involvement.

Neuroblastoma is derived from the neural crest ectoderm and is the malignancy of sympathetic nervous system. The tumor cell can produce and excrete cathecholamines substances such as dopamine, epinephrine and its metabolites - vanillylmandelic acid (VMA) and homovalnillic acid (HVA).[11,13] About 90-95% of neuroblastoma cases have high urine VMA and HVA at diagnosis. If the ratio between urine HAV and VMA is more than 1.5, it is a good prognosis.[11,13] Because the tumor cell can excrete epinephrine which can be detected in plasma, this can cause severe systemic hypertension at diagnosis.[14] The neuroblastoma cell can produce and excrete other substances such as neurone-specific enolase (NSE), vasoactive intestinal peptide (VIP), ferritin and lactic dehydrogenase (LDH).[11,13] As in our patient, serum NSE is very high. NSE is the tumor marker for neuroblastoma. It is useful for following the disease activity and the response to treatment in individual patients.[11,13]

Ultrasound is a useful screening modality in the evaluation of abdominal neuroblastoma. The ultrasound appearance of prenatal adrenal neuroblastoma are variable. It could show cystic, mixed cystic and solid, completely solid or hyperechoic masses as in this case and even the foci of calcification.[10] In our case, postnatal ultrasound showed solid bilateral suprarenal masses and hepatosplenomegaly. The differential diagnosis by ultrasound included adrenal hemorrhage and congenital neuroblastoma. The definite differentiation of hemorrhagic tumor from purely adrenal hemorrhage may be difficult.[4,5] Color Doppler ultrasound has been reported to showed increase flow in neuroblastoma.[15-16] The another way to differentiate adrenal hemorrhage from neuroblastoma is close

follow up with serial sonography. Adrenal hemorrhage will demonstrate change in echogenicity and decrease size on follow up sonograms.[17] The CT scan is the modality of choice for diagnosis the patients suspected neuroblastoma. The CT scan can demonstrate all accurate primary tumors and metastatic lesions. Abdominal neuroblastoma typically appears on CT as irregular suprarenal masses with a heterogeneous texture due to hemorrhage and necrosis. Calcified is detected in 85% of cases.[18-19]

Another rare complication of congenital neuroblastoma is disseminated intravascular coagulation (DIC). A few reported cases of congenital neuroblastoma with DIC are found in the literature.[20-22] The infant were very young with metastases to liver, bone marrow and the other adrenal gland. DIC was assumed to be secondary to thromboplastin release from the tumor.[17]

Conclusion

Congenital bilateral neuroblastoma is quite rare. It can present with abdominal masses, hemorrhagic complication, DIC and hepatic failure in the neonatal period. The sonography could show cystic or mixed cystic and solid suprarenal mass. CT scan can well demonstrate primary tumor and metastatic lesions.

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สาขาโลหิตวิทยาและมะเร็ง ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

บทคัดย่อ: *ผู้เขียนรายงานผู้ป่วยทารกแรกเกิดเพศชาย 1 ราย มาด้วยอาการซีด ก้อนในท้อง ภาวะเลือดออกรุนแรง มีภาวะเกิดลิ่มเลือดอุดตันทั่วไป (DIC) และตับวาย จากการตรวจอัลตราซาวน์ช่องท้องพบ ก้อนที่บริเวณเหนือไตทั้งสองข้าง ก้อนเป็นลักษณะก้อนแข็ง ผู้ป่วยเสียชีวิตจากภาวะเลือดออกที่ไม่สามารถควบคุมได้ ตับวายและไตวาย ผลจากการชันสูตรหลังเสียชีวิต พบว่าเป็น นิวโรบลาสโตมาที่ต่อมหมวกไตทั้งสองข้าง ร่วมกับมีการกระจายไปที่ตับ ปอด ต่อมไทมัส และต่อมน้ำเหลือง โดยไม่พบการกระจายไปที่ไขกระดูก การวินิจฉัยในผู้ป่วยรายนี้คือ นิวโรบลาสโตม่าที่เป็นมาแต่กำเนิด ขั้นที่ 4 โรคนี้พบได้น้อยมาก ควรพิจารณาการวินิจฉัยโรคนี้ เมื่อพบผู้ป่วยแรกเกิดที่มีก้อนในช่องท้องร่วมกับมีภาวะเลือดออกรุนแรงและตับวาย*

Key Words : ● *Congenital neuroblastoma* ● *Hepatic failure*

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