Cystic Neuroblastoma in Infancy: a report of 3 cases

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We present a report of three patients of cystic neuroblastoma who aged 23 days, one year and 3 months respectively. Two of the three patients presented with fever of unknown origin and the third patient with abdominal mass clinically. CT scans show cystic masses with internal septation in the adrenal area in all three patients.

Key words: Adrenal gland, CT; Neuroblastoma

Neuroblastoma is the most common malignant solid tumor in infants less than 1 year old; however cystic neuroblastoma is exceedingly rare. Along with progress in prenatal diagnosis by ultrasound, an increasing number of cystic neuroblastomas had been reported [1]. We present the following report of three patients with cystic adrenal neuroblastoma.

**CASE REPORT**

**Case 1**

A newborn baby was admitted to hospital at the age of 23 days old with fever of unknown origin up to 39°C. The female newborn was born by a G2P2 healthy mother by caesarean section at 40 week’s gestation in a local clinic and weighed 3600 gm. The perinatal examination was unremarkable. Delivery course was smooth. Septic workup was arranged but no definite pathogen was identified. On physical examination, the patient was pale and a palpable abdominal mass was noted. Abdominal ultrasound showed a cystic mass cephalic to left kidney. Abdominal CT showed a well-defined mixed density mass lesion occupying the left upper abdomen on pre-contrast study. Marginal enhancement with central septation and cystic component in the lesion which caused external compression to upper pole of left kidney were seen on enhanced study (Fig. 1a, 1b). The density of the cystic compartment and the densities of wall in the precontrast and postcontrast studies were listed in Table 1, respectively. Laboratory investigations showed hemoglobin was 8.0 mg/dl and urine for vanillylmandelic acid (VMA) was within normal limit. At surgery, a left adrenal cystic lesion was measured about 9x6x6 cm which was encapsulated and firmly adhered to superior mesenteric artery (SMA), pancreas and left renal hila. Total removal was performed. Microscopically, the encapsulated tumor had hemorrhage, necrosis and cystic change, and acute inflammatory exudate was present in the cystic cavity. Schwannian stroma or ganglion cells differentiation was not evident. Poorly
differentiated neuroblastoma was diagnosed by pathological findings (Fig. 1c). On immunohistochemistry, the tumor was positive for neuron specific enolase (NSE) (Fig. 1d) and chromogranin but negative for MIC-2 (CD-99) and synatophysin. Unfortunately, recurrence of left adrenal neuroblastoma with invasion of upper pole of left kidney and para-aortic lymphadenopathy were seen 6 months later.

**Case 2**

A one-year-old male baby presented with fever for 10 days. The past history was unremarkable. Septic workup was arranged but no definite pathogen was identified. Abdominal ultrasound showed a mass lesion occupying right side adrenal area. Abdominal CT showed an ill-defined iso to hypodensity mass lesion occupying the right upper retroperitoneum on pre-contrast study. Irregular marginal enhancement of the lesion which caused external compression to upper pole of right kidney was seen on enhanced study. (Fig.

<table>
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<th>Case</th>
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<td>Average (HU)</td>
<td>13.43</td>
<td>34.59</td>
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</tbody>
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HU: Hounsfield Units

**Figure 1. a,b,c,d.** Contrast enhanced CT scan of the abdomen in a 23-day-old female baby showed a large suprarenal mass with marginal enhancement, central septation and cystic component, which caused external compression to upper pole of left kidney. c. Neuroblastoma, Schwannian stroma-poor, poorly differentiated subtype. It is composed of small neuroblastoma cells separated into lobules by delicate fibrovascular septa. Neuropil is clearly recognizable in the background. (Hematoxylin and eosin, magnification x200). d. The neuroblastoma cells show strong immunoreactivity for neuron specific enolase.
2a) The density of the cystic compartment and the densities of wall in the precontrast and postcontrast studies were listed in Table 1, respectively. Laboratory investigations showed hemoglobin 10.1 mg/dl and urine VMA was within the normal limit. Laparotomy was performed. At surgery, dense fibrous bands and fat adherent to the renal capsule were sharply divided by diathermy and a cystic adrenal mass was almost totally removed. Poorly differentiated neuroblastoma was diagnosed by pathological findings (Fig. 2b). Microscopically, the encapsulated tumor had hemorrhage and necrosis. A small defect was seen in the capsule of the tumor. Unfortunately, recurrence of right adrenal neuroblastoma was seen 8 months later.

Case 3

A 3-month-old female baby was presented with abdominal mass. The female infant was born by a G2P2 healthy mother with gestational age of 38 weeks. The birth body weight was 3200 gm. The perinatal course was smooth. On physical examination, a palpable abdominal mass occupying left upper

Figure 2. a. Contrast enhanced CT scan of the abdomen in a one-year-old male baby showed a cystic mass with an enhanced thickened wall in the right suprarenal area. b. Neuroblastoma, Schwannian stroma-poor, undifferentiated subtype, composed of undifferentiated neuroblastic cells without discernible neuropil in the background. (Hematoxylin and eosin, magnification x200)

Figure 3. a. Contrast enhanced CT scan of the abdomen in a 3-month-old female baby showed a huge suprarenal mass with marginal enhancement, central septation and cystic component, causing external compression to upper pole of left kidney. b. Neuroblastoma cells with fibrillary matrix. (Hematoxylin and eosin, magnification x200)
abdomen was noted. Abdominal ultrasound showed a huge cystic mass found in left suprarenal area. Abdominal CT showed a well-defined iso to hypodensity mass lesion occupying the left upper abdomen on pre-contrast study. Marginal enhancement with central septation and cystic component in the lesion which caused external compression to upper pole of left kidney were seen on enhanced scan. (Fig. 3a) The density of the cystic compartment and the densities of wall in the precontrast and postcontrast studies were listed in Table 1, respectively. Laboratory investigations showed urine for VMA was within normal limit. At surgery, a huge left adrenal cystic lesion was totally removed. Microscopically, Schwannian stroma or ganglion cells differentiation was not evident. Adrenal neuroblastoma with stage I was diagnosed (Fig. 3b). There was no evidence of tumor recurrence on the follow-up examinations.

**DISCUSSION**

Neuroblastoma commonly presents with a palpable abdominal mass, abdominal pain, fever, and bone pain and less commonly with myoclonus, opnoclonus, cerebellar ataxia, orbital ecchymosis or intractable diarrhea [2]. Clinically, two of our three cases presented with fever of unknown origin initially and a palpable abdominal mass found incidentally in the third patient. The urine vanillylmandelic acid (VMA) levels of the three patients were all within the normal limit.

In general, solid neuroblastomas cause elevated VMA, homovanillic acid (HVA), and neuron-specific enolase (NSE) but most cystic neuroblastomas are nonfunctional tumors [1] that are composed of only a small portion of solid tissue [3]. Moreover, radiiodinated metaiodobenzylguanidine (MIBG) scintigraphy is reported with high sensitivity and high specificity in detecting solid neuroblastomas [4] but two cases of cystic neuroblastoma show no positive finding from previous reports [5, 6]. MIBG scintigraphy may be useless in detecting cystic neuroblastoma due to few solid components.

The image presentations of these three cases of adrenal cystic neuroblastoma show well-enhanced thickened wall on CT scan. One of the images shows irregular thickened wall while the other two show smooth thickened wall with central septation. According to Croitoru [7], a cystic adrenal mass with irregular, thickened wall should be highly suspicious for cystic neuroblastoma.

The other differential diagnoses of suprarenal cystic lesions in newborn include adrenal hemorrhage, adrenal cyst, duplicated kidney with cystic change, cystic Wilms’ tumor, mesoblastic nephroma, infradiaphragmatic pulmonary sequestration, hepatic cyst, neurogenic cyst and choledochal cyst. Adrenal hemorrhage is a common cause of an adrenal cystic lesion especially in the newborn. Cystic neuroblastoma has been thought to occur secondary to hemorrhage into a neuroblastoma. Differentiating cystic neuroblastoma from fetal adrenal hemorrhage may potentially be difficult [1]. The follow-up ultrasound examinations may provide a clue to differentiate cystic neuroblastoma from adrenal hemorrhage by more complex echogenicity [8]. Vessels are demonstrated within the cystic neuroblastoma by color coded Doppler sonography and power Doppler sonography [9].

However, differentiating adrenal hemorrhage from cystic neuroblastoma would be difficult occasionally. The enhancement pattern of a cystic mass on postcontrast CT study would be a clue for differentiating these two lesions. Therefore, we think that CT may play a role in the pre-operative diagnosis for cystic neuroblastoma.

**REFERENCE**

幼兒之囊狀神經母細胞瘤：三病例報告

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我們報告三個囊性神經母細胞瘤的幼兒病例，年紀分別為23天，一歲及三個月，臨床表現上，有兩個以不明熱來表現，另一個則以腹部腫瘤來表現，斷層掃描的表現均在腎上腺有囊性變化。

關鍵詞：腎上腺，電腦斷層，神經母細胞瘤