

## Case report

# Congenital bilateral cystic neuroblastoma with liver metastases and massive intracystic haemorrhage

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**Abstract.** A case of bilateral cystic neuroblastoma with liver metastases in a newborn is reported. CT showed a 10 cm right suprarenal multicystic mass and numerous hepatic cystic masses with intracystic fluid–fluid levels. Multiple smaller cystic lesions were also present in the left adrenal gland. To our knowledge, the CT findings of neonatal bilateral cystic neuroblastoma with liver metastasis and massive acute intracystic haemorrhage has not been previously documented.

Neuroblastoma is one of the most common malignant tumours of infancy and childhood, with 40–50% of cases arising in the adrenal glands [1–4]. Neuroblastomas with bilateral adrenal involvement comprise about 10% of cases [5, 6]. Cystic neuroblastomas are uncommon [7–12] and only one case of bilateral cystic neuroblastoma has been described [7]. Although intratumoral haemorrhage is common in neuroblastoma, massive symptomatic haemorrhage is rare [6]. We report the CT findings of an extremely rare case of neonatal bilateral cystic neuroblastoma with liver metastases and massive acute intracystic haemorrhage causing marked anaemia.

## Case report

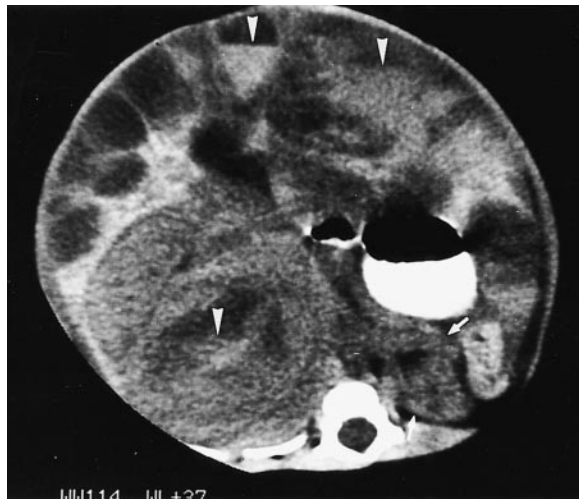
A baby girl was admitted to hospital at the age of 8 h with marked abdominal distension. She was born by caesarean section at 41 weeks' gestation in a local clinic. She weighed 4850 g and had Apgar scores of 8 and 10 at 1 and 5 min. Maternal history (28-year-old, gravida 3, para 3) was unremarkable. Prenatal ultrasound at 37 weeks' gestation had shown an increased fetal abdominal circumference but no abdominal mass was reported. On physical examination, the patient was pale and tachypnoeic. The abdomen was markedly distended and was difficult to examine. The pulse rate was 147 per min, respiratory rate 63 per min and blood pressure was 57/30 mmHg. Abdominal ultrasound showed multiple complex masses in the liver and right renal fossa. Laboratory investigations showed

haemoglobin 6.6 g dl<sup>-1</sup> with mean corpuscular volume 113 fl and white blood count 20.6 × 10<sup>9</sup> l<sup>-1</sup> with 70% polymorphonuclear leucocytes. Abdominal CT showed a 10 cm multicystic haemorrhagic mass in the right suprarenal region displacing the right kidney inferiorly, numerous haemorrhagic hepatic cystic masses with rim enhancement, and multiple smaller cystic lesions in the left adrenal gland (Figure 1). The haemoglobin level dropped to 4.4 g dl<sup>-1</sup> the next day and packed red blood cells and fresh-frozen plasma were transfused. Spot urine vanillylmandelic acid (VMA) was mildly elevated.

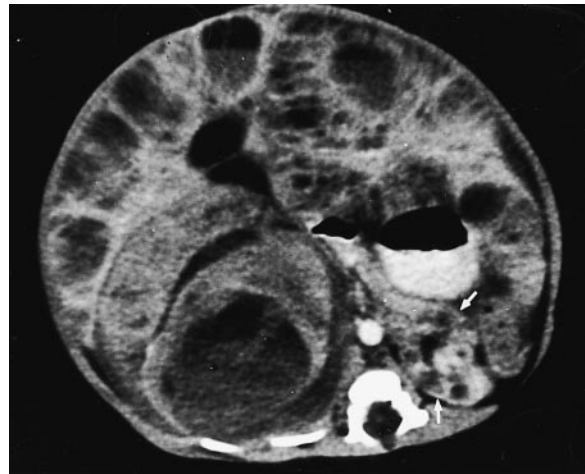
At surgery, a 10 cm well defined, reddish, multicystic right adrenal mass was seen. The left adrenal gland was slightly enlarged with multiple small cystic lesions and was preserved. Hepatomegaly with multiple cystic tumours was found. Resection of the right adrenal mass and a wedge liver biopsy were performed. On sectioning, the tumour appeared encapsulated and multicystic with marked haemorrhagic necrosis. Microscopically, the adrenal tissues were infiltrated by nests of small hyperchromatic cells. Extensive haemorrhage, necrosis and cystic degeneration were noted. The pathological findings of the liver biopsy were similar. On immunohistochemistry, the tumour was negative for cytokeratin, chromogranin A, neurofilament, synaptophysin and periodic acid-Schiff stainings but was positive for neuron-specific enolase. N-myc oncogene expression and DNA flow cytometry were not obtained. A bone marrow study showed no tumour cells. A radionuclide bone scan was negative. A diagnosis of adrenal neuroblastoma with liver metastases (stage IV-S) was made. The post-operative course was smooth. Unfortunately, the patient's parents refused chemotherapy and the patient was lost to follow-up after discharge.

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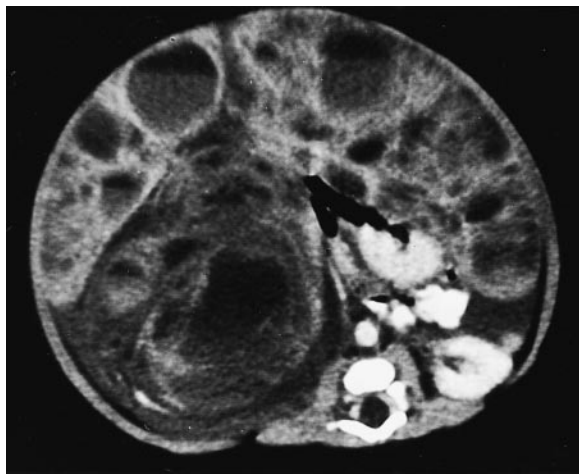
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(a)



(b)



(c)

**Figure 1.** (a) Unenhanced CT scan shows a large heterogeneous right suprarenal mass and multiple hepatic cystic lesions with high density fluid–fluid levels (arrowheads). Note thickened lateral and medial crura of the left adrenal gland (arrows). Contrast enhanced CT scans at the levels of (b) the left adrenal glands and (c) the mid-portion of the left kidney show prominent rim enhancement of the multicystic right adrenal mass and hepatic cystic lesions. Multiple left adrenal cystic lesions are also seen (arrows).

## Discussion

Neuroblastomas are derived from the neural crest ectoderm and are the most common solid abdominal masses of infancy. 75% affect children younger than 4 years with an incidence of 1 per 10 000 to 1 per 100 000 live births [1–5]. Bilateral adrenal neuroblastoma, occurring in 10% of the cases, may represent a second primary tumour or a contralateral metastasis [5–6]. Congenital neuroblastoma is uncommon and about 80 cases have been described [7–13]. Cystic neuroblastomas are even rarer and only 33 cases have been reported [7–12]. Bilateral cystic neuroblastoma is extremely unusual and, to our knowledge, there has been only one other documented case in the literature [7]. The present case demonstrated a great discrepancy in sizes between the left and right adrenal tumours, with a large multicystic adrenal mass on the right and multiple smaller cystic masses on the left. However, it is impossible to make a definitive differentiation between synchronous bilateral primary adrenal tumours and contralateral metastasis. Thus, a presumptive stage IV-S was made. If the left adrenal lesions

were due to metastasis, the tumour staging would be regarded as stage IV. Neuroblastoma can metastasize *in utero*. When present, as in our case, the fetal liver is the most common site with nearly total replacement of the liver parenchyma. Other sites include the placenta, retroperitoneal nodes, paraspinal region, bone, skin and umbilical cord [5, 10, 12, 13].

Neuroblastoma may be a microscopic *in situ* tumour or a grossly recognizable neoplasm. Nodules of neuroblasts may be found in all adrenal glands of fetuses at 17–30 weeks' gestational age. Perinatal autopsy studies reported that neuroblastic nodules or neuroblastoma *in situ* occur in approximately 1 per 200–250 cases, much higher than the expected incidence. Only a small proportion of the neuroblastic nodules may develop into clinically significant neuroblastomas [5, 12, 14]. Neuroblastomas commonly present with a palpable abdominal mass, abdominal pain, fever and bone pain, and less commonly with myoclonus, opsoclonus, cerebellar ataxia, orbital ecchymosis or intractable diarrhoea [1, 4]. Although intraglandular or intratumoral haemorrhage is common,

massive symptomatic haemorrhage is rare [1, 6]. A case of massive haemoperitoneum due to rupture of a haemorrhagic neuroblastoma has been reported [6]. Our case illustrated a unique manifestation of acute massive haemorrhage of cystic neuroblastoma and its hepatic metastatic lesions, along with rapid worsening anaemia.

Ultrasound is a useful screening tool in the evaluation of abdominal neuroblastoma. Since the prenatal ultrasound was performed elsewhere in this case, we do not know whether the adrenal or hepatic masses were overlooked or whether there were rapid-growing abdominal tumours during the last 3 weeks of gestation. The ultrasound appearances of perinatal adrenal neuroblastoma are variable and range from cystic, mixed cystic and solid, to completely solid or hyperechoic masses, even containing foci of calcification [7–13]. In this case, postnatal ultrasound showed complex masses in the liver and right renal fossa. However, the left adrenal cystic lesions and intracystic haemorrhage were not recognized. Definitive differentiation of haemorrhagic cystic tumour from purely adrenal haemorrhage or adrenal abscess may be difficult [7, 8, 11]. CT is the modality of choice for patients with neuroblastoma with its accurate depiction of all primary tumours and metastatic lesions [1–4, 15]. Abdominal neuroblastomas typically appear on CT as irregular suprarenal masses with a heterogeneous texture due to haemorrhage and necrosis. Calcification is detected in 85% of the cases [1–4]. On the other hand, perinatally diagnosed neuroblastomas are frequently cystic [12, 13]. The cyst content may be serous, gelatinous or haemorrhagic [6–13]. In addition to cystic neuroblastoma, the differential diagnosis of suprarenal cystic masses in infants includes adrenal haemorrhage, obstructed upper moiety of a duplex kidney, adrenal abscess, adrenal cyst, enteric cyst, cystic Wilms' tumour, mesoblastic nephroma, a multilocular cystic nephroma, extralobar sequestration and choristoma [6–12]. In this case, CT offered a specific diagnosis of intracystic bleeding by demonstrating the high density fluid–fluid levels within the cystic lesions. Rim enhancement of the lesions raised the possibility of cystic tumours. The occurrence of multiple hepatic lesions was indicative of metastasis *in utero*, reflecting that the right adrenal mass or bilateral adrenal masses might be the primary malignancy. Detailed evaluation of the distorted right kidney was also helpful in excluding renal tumours. Therefore, despite the rarity, bilateral

cystic neuroblastoma with liver metastasis and massive intracystic haemorrhage was the most pertinent entity that can fit the clinical and imaging characteristics disclosed in this case.

Surgery is the treatment of choice when excision of the tumour seems feasible. Chemotherapy is necessary for more advanced tumours or metastases. Radiotherapy may be applied for unresectable or incompletely excised tumours [1].

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