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Congenital neuroblastoma mimicking early onset sepsis

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Abstract A newborn girl presented with symptoms of severe early onset sepsis but also with systemic hypertension (SH) at age 3 h. Plasma catecholamine (CAT) levels were extremely elevated, reflecting increased release of CAT from a congenital neuroblastoma (NB). Clinical symptoms at time of admission were: prolonged capillary refill (5 s), tachycardia, tachypnoea, metabolic acidosis (pH 7.17, lactate 11.8 mmol/l), fever (38.4 °C) and SH: 90/50/65 mmHg (systolic/diastolic/mean). The infant experienced organ failure (lung, heart, liver). A retroperitoneal dumbbell tumour was detected. Plasma CAT levels at age 15 h were: noradrenaline 219 nmol/l; adrenaline 13 nmol/l; and dopamine 65.3 nmol/l. SH responded to intermittent α-adrenergic blockage. CAT-related symptoms ceased within 1 week. The intraspinal NB was surgically removed when cord compression became symptomatic. The neurological and developmental state is normal at age 17 months. The abdominal NB regressed spontaneously.

Conclusion A neuroblastoma should be considered in newborn infants presenting with a shock-like condition together with systemic hypertension.

Key words Congenital neuroblastoma · Plasma catecholamines · Systemic hypertension

Abbreviations CAT catecholamines · NB neuroblastoma · SH systemic hypertension

Introduction

Neuroblastoma (NB) is a common malignant tumour of the newborn. NB cells may produce catecholamines (CAT), but usually only the inactive metabolites are increased in blood and urine. However, maternal systemic hypertension (SH) has been reported in fetal NB [7], one neonate with NB and SH died at age 12 days [12], and high plasma CAT levels have been described in one other infant with NB and SH during the first weeks of life [9]. We report on a neonate with NB and extremely elevated plasma CAT levels mimicking early onset sepsis with life-threatening organ failure immediately after birth.

Case report

The mother was normotensive. Preterm labour and vaginal delivery started at 34.2 weeks of gestation. Fetal heart rate was 130 bpm, umbilical arterial pH was 7.40 and Apgar score was 7 at 5 min. The infant suffered from tachypnoea (80 min⁻¹). The skin appeared cyanotic while the transcutaneous oxygen saturation was 0.90. Interleukin 8 (< 5 ng/l), C-reactive protein (< 4 mg/l) and leucocytes (8.7 g/l) were normal. The suspected diagnosis at time of admission (age 3 h) was early-onset sepsis.

The body temperature was 38.4 °C. The heart rate (182 bpm) and blood pressure (90/50/65 mmHg, systolic/diastolic/mean, Dinamap oscillometry) were increased [13] in contrast to the prolonged capillary refill time (5 s). The infant looked pale and livid in spite of an oxygen saturation above 0.9. An abdominal mass, which was first interpreted as an enlarged liver, reached 7 cm below the
right lower costal margin. Metabolic acidosis was present (pH 7.14; base deficit -11.8) with a maximum lactate of 13.4 mmol/l (age 9 h), decreasing to 4.8 mmol/l at age 21 h. pCO₂ and FiO₂ were 6.9 kPa and 0.21 respectively and increased to 8.3 kPa and 0.6 within 1 h. The prothrombin time (28.8 s) increased to 45.2 s at age 21 h. Fresh frozen plasma was substituted until day 5. Leucocyte count was 18.7 g/l and ratio of immature to total granulocytes 0.33. Haematocrit (0.69) was elevated. Maximum creatinine was 140 µmol/l. Normal values were found for blood glucose, serum electrolytes, protein, ammonia, pyruvate, T₃, T₄, TSH, TSH receptor antibodies, platelets and C-reactive protein. Blood culture was sterile.

The chest X-ray film showed a marked homogeneously decreased radiolucency with air bronchogram. Left ventricular shortening fraction (echocardiography) decreased from 35% to 21% (normal: 28% - 44%) within 17 h. On abdominal sonography, a retroperitoneal tumour (5.9 x 4.0 x 3.6 cm) was found with small hyperdense areas and intraspinal extension, compressing the spinal cord at the level of T12. Plasma CAT levels are given in Table 1. Homovanillic and vanillylamandelic acid were increased in the urine: 222.2 nmol/μmol creatinine and 223.5 nmol/μmol creatinine (normal upper limit: 25.3 and 18.1 nmol/μmol creatinine). Neuron specific enolase was >200 ng/ml (normal upper limit 24.8 ng/ml). MRI confirmed the sonographic results. No metastases were found (bone marrow aspirations, meta-iodobenzylguanidine scan).

Mechanical ventilation was initiated (peak inspiratory pressure 20 cm H₂O, positive end-expiratory pressure 6 cm H₂O). The FiO₂ of 0.6 was reduced to 0.21 without surfactant therapy within 12 h and the infant was weaned off the ventilator on day 6. Morphine and phenobarbital were given. Metabolic acidosis was treated with 6.4 mval/kg sodium bicarbonate. Antibiotic therapy was discontinued when the diagnosis of NB was confirmed by sonography and C-reactive protein remained negative. Volume load did not improve the capillary refill. Central venous pressure varied from +3 to +7 cm H₂O. Diuresis started at age 18 h. A synopsis of data on heart rate, blood pressure and interventions is given in Fig. 1.

Treatment of the NB was performed according to the protocol (NB 97) of the German Co-operative Multicenter Trial (study co-ordinator F. Berthold). Since the onset of palsy of the legs was detected after morphine had been antagonised with naloxone, the major part of the intraspinal NB was removed by hemi-laminectomy. Histology was favourable [11] and N-myc amplification was negative. The patient was assigned to the surveillance group without chemotherapy according to the NB 97 protocol.

The CAT-related symptoms ceased within 1 week. Systolic blood pressure (73–104 mmHg, [2]) and the neurological and developmental state were normal at regular presentations until the present age of 17 months. The abdominal NB regressed and homovanillic and vanillylamandelic acid in the urine decreased (day 24: 75.4 and 102.1 nmol/μmol creatinine) and have been normal since the age of 7 months. A meta-iodobenzylguanidine scan was normal at age 14 months.

**Discussion**

The clinical features of the patient mimicked those of severe early onset sepsis but SH did not fit this diagnosis.

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**Table 1** Plasma CAT levels in the patient with congenital NB at ages 15 h and 2 months and together with reference data from [6] and [8]

<table>
<thead>
<tr>
<th>Patient</th>
<th>Noradrenaline (nmol/l)</th>
<th>Adrenaline (nmol/l)</th>
<th>Dopamine (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 15 h</td>
<td>219.0</td>
<td>13.0</td>
<td>65.3</td>
</tr>
<tr>
<td>Age 2 months</td>
<td>6.5</td>
<td>1.1</td>
<td>0.54</td>
</tr>
<tr>
<td>Reference data in umbilical arterial blood (mean ± SEM)</td>
<td>27.7 ± 15.1</td>
<td>3.2 ± 1.3</td>
<td>2.8 ± 1.1</td>
</tr>
<tr>
<td>Reference data during mechanical ventilation (median and interquartile range)</td>
<td>11.0 (6–20)</td>
<td>1.0 (0.4–1.9)</td>
<td></td>
</tr>
</tbody>
</table>

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**Fig. 1** Synopsis of heart rate, blood pressure, diagnostic interventions and therapy. Volume (vertical arrow) 10–15 ml/kg given in 15 min, blood sample (cross) for plasma catecholamines, blood and urine sample (double cross) for neuron specific enolase and catecholamine metabolites. (BP blood pressure (mmHg), Cap. Refill capillary refill time (s), HR heart rate (bpm), IPPV intermittent positive pressure ventilation, N application of naloxone hydrochloride)