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Low cord blood levels of catecholamine from a newborn of a pheochromocytoma patient

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Association of pheochromocytoma and pregnancy is rare and usually related to high maternal and fetal mortality rates. Maternal effects of the tumor have been studied extensively and the clinical outcome has markedly improved during the last decade. However, the role of excess catecholamines on fetal development has been discussed very little. We report here a case of pheochromocytoma during pregnancy, in which catecholamine levels from the cord blood were low despite simultaneous elevated maternal values (1.93 and 29.46 nmol/l norepinephrine, respectively), possibly owing to the high activity of the catecholamine degradative enzymes monoamine oxidase and COMT at the placental level. We suggest that in pregnancies complicated by pheochromocytoma, fetal well-being may be related mainly to good control of maternal blood pressure instead of to the amount of catecholamines in the fetal circulation, because the placenta performs a protective role through an effective process of hormone inactivation.

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Pheochromocytoma may be a rare complication of pregnancy, associated with high maternal and perinatal mortality rates (1, 2). Medical treatment using α- and sometimes also β-adrenergic antagonists has decreased both maternal and fetal risks, leading to a successful outcome in a significant number of cases when treated correctly (3).

Most situations associated with fetal damage are related to hemodynamic changes in placental vessels (4, 5) secondary to maternal hyperadrenergic status. However, little is known (1–4) about possible direct effects of high catecholamine levels on fetal development.

The successful management of a pheochromocytoma during pregnancy with measurement of catecholamine levels from cord blood is described and a brief discussion of the placenta's role as an effective barrier to catecholamine transfer to fetal blood is presented.

Case report

A 39-year-old female was referred to our service in the 24th week of her 8th pregnancy complaining of paroxysmal episodes of sweating, headache and palpitations, accompanied by high blood pressure. Her last gestation occurred 7 years previously and she reported hypertension only during labor. She had not been treated since then. Her family history was unremarkable. On physical examination, her supine blood pressure was 150 × 100 mmHg with postural hypotension and the obstetric features were compatible with the gestational age ascribed. A magnetic resonance imaging scan disclosed an 8-cm mass in her right adrenal gland. Pheochromocytoma diagnosis was established by the finding of high urinary excretion of VMA (257.34 μmol/day; normal, < 60.55 μmol/day) and metanephrines (19.1 μmol/day; normal, 0.27–6.54 μmol/day). Catecholamines were measured by HPLC with electrochemical detection, as described previously (6). Plasma samples were collected in iced tubes after at least 30 min of vein puncture. The tubes containing 5 pg of EGTA and 9 pg of glutathione were separated immediately by centrifugation at refrigerated conditions and maintained at −70°C until assayed. Urinary and plasma levels also were elevated unequivocally: urinary norepinephrine (NE), 9652.66 nmol/day (normal, 82.75–472.88 nmol/day); epinephrine (E), 231.96 nmol/day (normal, 2.72–109.16 nmol/day). The plasma NE level was 65.84 nmol/l (normal, 0.23–1.58 nmol/l) and the E level was 1.17 nmol/l (normal, <0.41 nmol/L). Hypertension was treated with α_1-selective adrenergic antagonist prazosin but, despite the use of high doses (up to 20 mg/day), some hypertensive chrises still occurred. Fetal status was assessed by serial biophysical profile determination, and no significant abnormalities were found. Considering the high risk of labor in this condition and because the patient had some uterine contractions, gestation was terminated at the 34th week. During the cesarean section, blood samples were collected simultaneously from a peripheral vein of the mother and from cord blood for catecholamine assay. The mother's NE and E levels were 29.46 and 0.37 nmol/l, respectively, while the cord levels of NE were 1.93 nmol/l and the E levels were

Table 1. Maternal and cord blood levels of norepinephrine and epinephrine in 20 normal controls during cesarean section.[a]

	Norepinephrine (nmol/l)	Epinephrine (nmol/l)
Mother	1.4±0.68 (0.33–2.57)	0.51±0.61 (0.09–2.03)
Cord Blood	22.93±42.46 (1.43–150.84)	2.27±3.79 (0.15–16.78)

[a] Values are means±SD, with range values in parentheses.

undetectable. A female child was born with good cardiovascular and respiratory conditions. The tumor was excised surgically 10 days later and histopathological studies confirmed pheochromocytoma. After the procedure, the patient's blood pressure normalized as well as catecholamines levels (NE, 1.59 nmol/l; E, 0.42 nmol/l). Both mother and child's outcome were uneventful, and they were discharged together 2 weeks later.

Discussion

The maternal consequences of the association of pheochromocytoma and pregnancy have been discussed extensively (1–5). However, the effects of excess catecholamines on the fetoplacental unit have received very few considerations in recent publications. The scarce reports available mainly describe obstetric complications due to vasoconstriction of the uteroplacental bed (4, 5, 7) and potential secondary effects of antihypertensive drugs used by the mother (8–10), with no references to the catecholamine status of the fetus or newborn infant.

It is believed that, in humans, a small amount of catecholamines may be transferred to the fetus through the placental barrier (11, 12). In the present case, an amount equivalent to only 7% of maternal NE levels was detected in cord blood during birth. This finding is in agreement with experimental studies performed in animals (11–13), in which fetuses of mothers exposed to high amount of adrenergic hormones showed low levels of circulating catecholamines. This may be attributed to high monoamine oxidase (MAO) and (COMT) activity at the placenta, resulting in metabolic inactivation of intact forms of catecholamines originated from the mother (12, 13). In humans, the level of the most abundant inactive metabolite of catecholamines, VMA, was found to be fivefold higher in the cord blood of one fetus than in the mother's peripheral blood (12), confirming the placenta as a major source of catecholamine catabolism.

We measured also the catecholamines from maternal and umbilical blood during 20 normal births (see Table 1) and the fetal levels did not parallel the maternal values. In fact, as maturity of the adrenergic system is complete by birth (12, 14), we believe that the maternal counterpart of the catecholamines detected in fetal blood actually may be lower than formerly supposed, most measured hormones originating from the fetus' own adrenergic system. This is in accordance with previous reports and our own data from normal controls (14–19), which have shown a wide range of cord blood catecholamines at birth, related to different fetal conditions (15–18). The relatively low cord levels of catecholamines in our case may be attributed to the fact that this was a preterm child.

We were not able to obtain cord samples as well as the maternal samples of catecholamines during any of the pheochromocytoma chrises and, except for artificial experiments simulating hyperadrenergic conditions (20, 21), the effects of exceedingly high catecholamine levels, as might occur during adrenergic chrises of the pheochromocytoma, are not well described in humans.

Our findings support previous data from animal experiments, confirming the placenta's role as a catecholamine inactivator. This case suggests that in pregnancies complicated by pheochromocytoma, control of maternal blood pressure seems to have a critical role in fetal outcome; less importance should be attributed to the direct hazardous effects of catecholamines present in the fetal circulation.

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