A reason to panic in pregnancy

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An 18-year-old woman presented to us in June, 2004, at 27 weeks' gestation with aproteinuric hypertension (178/111 mm Hg) and intermittent panic attacks (palpitations, left abdominal pain, and perspiration). 24-h urinary catecholamine excretion was >20 000 nmol. Ultrasonography showed a 6·9 cm×3·6 cm×4·6 cm structure obscuring the left adrenal gland. Haemodynamic stability was achieved with phenoxybenzamine and labetolol, for the presumptive diagnosis of phaeochromocytoma. A staging CT was undertaken before elective caesarean at 37 weeks'; a healthy infant was delivered. The tumour was resected a month later. Histologically the tumour arose from the sympathetic paraganglion cells; the left adrenal gland itself was normal. Some vascular invasion was noted. DNA analysis showed *VHL* and *RET* genes to be normal, but there was a succinate dehydrogenase complex subunit B (*SDH-B*) gene mutation, predisposing her to paraganglioma syndrome type I. Postoperative ultrasound showed a 3·2 cm mass anterior to the inferior vena cava at the aortic bifurcation, but the patient declined further investigation.

She remained asymptomatic until the 32nd week of her next pregnancy, when flushing and palpitations were associated with rising urinary catecholamine secretions (to 4423 nmol/day). MRI showed that the mass had grown slightly to 3·5 cm. Despite an asystolic episode during caesarean section at term, the patient survived to undergo laparoscopic resection of the tumour 6 weeks' postpartum. Again, paraganglioma was identified histologically. The patient remained asymptomatic at follow-up in April, 2009.

Paragangliomas account for only 10–15% of catecholamine-secreting tumours. A large series put the prevalence of paraganglioma and phaeochromocytoma during pregnancy at five per million.[1] Maternal and fetal mortality are 4% and 11%, respectively,[2] which is related to delay in presentation and diagnosis. In pregnancy phaeochromocytomas may initially be missed, because the symptoms can mimic pre-eclampsia (table). Urinary catecholamine secretion and plasma metanephrines are not raised in normal pregnancy or pre-eclampsia and confirm the diagnosis of phaeochromocytoma.[3] Adequate medical management is required before delivery and surgery. Inpatient observation and management are recommended because of the unpredictable nature of phaeochromocytoma in pregnancy, although successful outpatient management was achieved when our patient declined admission. Resection should promptly follow medical stabilisation in cases diagnosed prior to 24 weeks'; after this time maintenance medical therapy should continue to optimise fetal maturity. Elective caesarean allows close monitoring and is the preferred mode of delivery since labour can be lethal. Planned caesarean also offers the opportunity for simultaneous tumour resection, but delaying this into the puerperium decreases vascularity and improves access. Germline mutations account for a quarter of phaeochromocytomas; commonly disease is of young onset and is multifocal or extra-adrenal.[4] Associated familial syndromes including Von Recklinghausen's disease, Von Hippel-Lindau disease, and multiple endocrine neoplasia types IIa and IIb. Mutations in *SDH-B*, *SDH-C*, and *SDH-D* genes account for 33% of patients with phaeochromocytoma due to genetic abnormalities. *SDH* genes code for discrete subunits of the mitochondrial enzyme complex II (involved in Kreb's cycle) and act as classic tumour suppression genes. *SDH-B* mutations are associated with a 33% risk of recurrence and malignancy,[4,5] and *SDH-D* mutations with an increased risk of multifocal paragangliomas, and renal and thyroid carcinomas. In women of reproductive age, genetic testing for one of the familial syndromes associated with phaeochromocytoma should be considered when there is family history of an associated syndrome, if the patient has any clinical features associated with a syndrome, or if the woman has extra-adrenal or multifocal disease. Although, the penetrance of *RET* and *VHL* is understood, the proportion of women with *SDH* mutations who develop clinical disease is unknown, complicating genetic counselling. Women known to have syndromes associated with phaeochromocytomas should receive pre-conceptual counselling about risks of disease developing during pregnancy.

	Phaeochromocytoma	Pre-eclampsia
Onset	At any point throughout pregnancy	Before 20 weeks' gestation unlikely
Hypertension	Paroxysmal	Persistent
Palpitations	Occur in 40%	Unlikely
Hyperhidrosis	Occur in 35%	Not a feature
Anxiety attacks	Occur in 18%	Unlikely

Table: **Comparison of phaeochromocytoma and pre-eclampsia characteristics in pregnancy**

Contributors
All authors were involved in managing the patient and writing the report.

References

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