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CASE REPORT

Multiple endocrine neoplasia type IIA (Sipple's syndrome) presenting in pregnancy

Jean V Joseph,[1] Robert Harrison,[2] and Robert S Davis[3]

Departments of Urology[1] and Endocrinology,[2] University of Rochester Medical Center,[3] Rochester, New York, United States of America

INTRODUCTION

Multiple endocrine neoplasia (MEN) type IIA, or Sipple's syndrome is a rare familial syndrome consisting of phaeochromocytoma, medullary thyroid carcinoma and parathyroid adenomas. Its occurrence in pregnancy is even rarer, with only 4 previous cases reported in the literature.[1,2,3,4] Phaeochromocytoma can easily go unrecognised since its signal symptom, hypertension, is present in several pregnancy associated diseases such as preeclampsia and eclampsia. An undiagnosed phaeochromocytoma can be catastrophic in pregnancy with maternal and fetal mortalities approaching 50%.[5] We report a case of MEN type IIA diagnosed in pregnancy, in which medical therapy allowed fetal maturation and elective Caesarian section, followed by bilateral adrenalectomies and thyroidectomy.

CASE REPORT

A 21-year-old primigravida with known uterine didelphus was noted to have a large left perirenal cystic lesion on a routine ultrasound at 16 weeks of gestation. A repeat abdominal ultrasound revealed a left adrenal mass measuring 9.1 x 8.6 x 7.4 cm and a 5 x 5 x 3 cm right adrenal mass. Magnetic resonance imaging (MRI) subsequently confirmed these tumours (Figure 1). No other tumours or abnormalities were found.

Endocrinological evaluation consisted of several 24-hour urine collections for homovanillic acid (HVA), 5.9 mg/24 hr (0–6.2 mg/24 hr) vanillyl mandelic acid (VMA), 21.4 mg/24 hr (0–6.8 mg/24 hr), normetanephrine 4.6 mg/24 hr (0–0.89 mg/24 hr), and metanephrines 10.6 mg/24 hr (0–0.39 mg/24 hr). Serum calcitonin was elevated at 37 pg/ml (0–6.3 pg/ml). Because of bilateral adrenal tumours, elevated catecholamines and elevated calcitonin, she was thought to have bilateral phaeochromocytomas and medullary thyroid carcinoma: MEN type IIA.

Address for correspondence

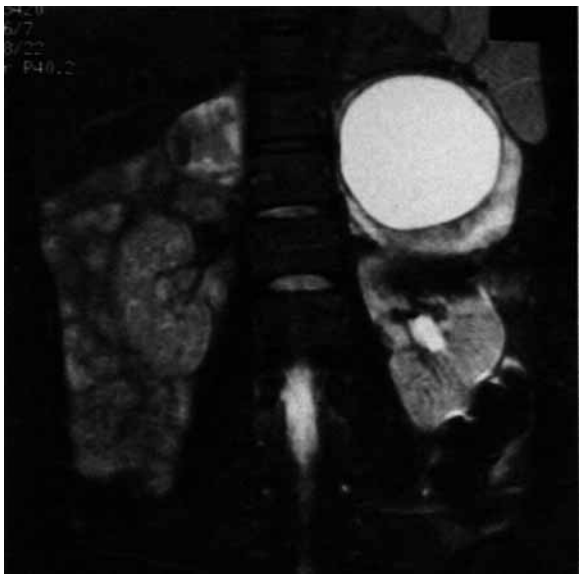
Jean V Joseph MD
Department of Urology
University of Rochester Medical Center
601 Elmwood Ave
Box 656 Rochester, New York 14642
United States of America

Jean V Joseph MD Assistant Professor, Robert W Harrison MD Professor, Robert S Davis MD Professor

Her pregnancy had been uneventful. She had been asymptomatic except for occasional panic attacks associated with palpitations. Her father had died in a car accident several years before and at autopsy was found to have bilateral phaeochromocytomas. None of the father's relatives, including the patient had been tested following this discovery. There was also a history of thyroid disease in the paternal grandparents.

The patient was admitted to the antenatal ward at 22 weeks gestation. Her blood pressure was 115/65 with a pulse of 90. Her abdomen was soft and non-tender with a uterine size consistent with gestational age. The remainder of her examination was unremarkable. She was started on intravenous fluids and given phenoxybenzamine which was titrated up by 10 mg per day while maintaining a stable blood pressure. The patient, was closely monitored by the obstetric, endocrine, and urologic teams. Because of significant risk to the mother, and the risk of preterm labour with a non-viable fetus, conservative medical management was continued. She was later discharged home at 24 weeks gestation on phenoxybenzamine 60 mg twice daily. At 26 weeks gestation, because of orthostatic hypotension,

Figure 1 Magnetic resonance imaging showing bilateral adrenal masses.



her regimen was changed to phenoxybenzamine 40 mg bid, and propanolol 10 mg tid which was well tolerated.

At 36 weeks of gestation, after an amniocentesis indicated adequate lung maturity, she underwent an uneventful low transverse Caesarean section under epidural anaesthesia. A 2728 g, footling breech, female infant with Apgars 9 and 9 at 1 and 5 minutes, was delivered from the left uterine horn. Her postpartum course was uncomplicated. Abdominal ultrasound on postpartum day 1 showed minimal adrenal changes. The left adrenal was 10.9 x 9.5 x 8.9 cm. The right was 5.5 x 5.9 x 3.8 cm. She was maintained on unchanged doses of propnanolol and phenoxybenzamine and discharged home on postpartum day four.

Eighteen days postpartum, the patient was readmitted and underwent bilateral adrenalectomies via a chevron incision. The larger left adrenal was first excised followed by the right with no complications. The pathology report confirmed the presence of bilateral phaeochromocytomas. She was started on a high dose of hydrocortisone which was later tapered. She was discharged on hydrocortisone 30 mg daily on postoperative day 4. A repeat serum calcitonin postpartum was 31 pg/ml (0–6.3). Six months postpartum, she underwent total thyroidectomy which revealed medullary carcinoma.

DISCUSSION

MEN IIA is a rare autosomal dominant disorder caused by a mutation in the RET oncogene on chromosome 10. Although medullary thyroid carcinoma is found in almost all patients, only 50% and 20% of them develop phaeochromocytomas and parathyroid adenomas respectively.[6] The phaeochromocytoma component of this disorder, if present, can lead to a poor outcome when undiagnosed in pregnancy. Maternal and fetal mortality, however, fall to zero and 15% respectively, when diagnosed in the prepartum period and managed prospectively.[7] Preeclampsia, eclampsia, and essential hypertension are often confused with phaeochromocytoma because of their similar presentations.

Our patient's adrenal masses were diagnosed by chance in the second trimester of her pregnancy on a routine staging ultrasound. Retrospective questioning, however, revealed that she had symptoms (palpitations and panic attacks) suggestive of a hypercatecholaminergic state. The measurement of urinary catecholamines was key in achieving an accurate diagnosis. MRI, which is non-invasive and avoids fetal radiation clarified the anatomy. In a recent review by Harper et al,[7] only 53% of the cases reviewed were diagnosed antenatally emphasising the need for increased detection efforts.

There is a lack of consensus in the literature regarding the management of phaeochromocytoma in pregnancy. Some advocate immediate removal regardless of the state of pregnancy. Others argue for surgical intervention only if the diagnosis is made before 23 weeks. After 24 weeks, surgery is delayed to allow fetal maturity with subsequent combined elective Caesarean section and tumour extirpation.[7] Nevertheless, there seems to be general agreement that such patients should be delivered electively by Caesarean section and not allowed to labour thus avoiding unmonitored stress. Our patient was managed with phenoxybenzamine and propranolol until fetal maturity was documented via amniocentesis.

A delay in the surgical removal of these tumours is best when they are bilateral, large, and can be managed medically, as in our patient. Allowing the gravid uterus to decrease its size postpartum helps in performing an adequate abdominal exploration, ruling out the presence of ectopic adrenal tumours. A chevron incision provides excellent access to both lesions and the sympathetic chain.

The diagnosis of MEN type IIA, or isolated phaeochromocytoma in pregnancy requires a high index of suspicion. Given a positive family history, screening of possibly affected relatives should be carried out with 24-hour urine catecholamine levels, in an effort to decrease further the associated mortality. This patient's excellent outcome illustrates the advantage of early diagnosis and multidisciplinary team management. Aggressive adrenergic blockade and careful monitoring allowed for safe delivery of a mature infant and the subsequent removal of two large phaeochromocytomas with no sequelae.

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