First reported case of ganglioneuroblastoma in pregnancy and a review of the literature

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Abstract

Ganglioneuroblastoma is a variant of neuroblastoma tumours with mature ganglion cell differentiation which occurs commonly in cervical, mediastinal and retroperitoneal locations. Approximately 90% of ganglioneuroblastomas are seen in children younger than five years old. There are 50 adult cases of ganglioneuroblastomas reported to date. Our patient is the 51st case and she is the first to be diagnosed in pregnancy. Our patient's tumour site was the thoraco-abdominal retroperitoneal space adjacent to her kidney. This tumour is generally diagnosed incidentally or by compression presentations, i.e. pain or neurological symptoms. Our patient's ultrasound scan appearances triggered suspicion of an atypical mass after presenting with loin pain. Caesarean section with tumour removal in the same session is preferred if tumour is small and localized. However in this case, there was uncertainty regarding the extent of the tumour. Therefore, the patient underwent thoracotomy after delivery to excise the thoraco-abdominal tumour, which extended from the level of the T9 to L2 vertebrae.

Keywords

Ganglioneuroblastoma, pregnancy, retroperitoneal mass

Introduction

Ganglioneuroblastoma is a variant of neuroblastoma tumours with prominent, mature ganglion cell differentiation.¹ They are mostly seen in the early childhood, especially less than five years old and are extremely rare in adults, with only 50 cases reported in adults over 20 years old.² Therefore, the clinical, radiographic and pathological features are poorly understood in adults.

To our knowledge, there are no reported cases of ganglioneuroblastoma presenting during pregnancy making our patient a challenging and interesting case.

Case presentation

A fit and healthy 21-year-old woman presented with a 24-h history of loin pain at 24 weeks' gestation whilst on holiday. She did not have symptoms of headache, palpitation, excessive sweating or dizziness. Her blood pressure (BP) was 120/80 mm of Hg.

Investigation

She had an ultrasound scan at 28 weeks demonstrating a 9 cm supra-renal mass with possible haemorrhagic changes. To explore the nature and extent of the lesion, a non-contrast magnetic resonance imaging (MRI) was performed at 30 weeks revealing an 8.1 × 7.3 cm right heterogeneous mass on T2 sequence deviating the right diaphragm, abutting the vertebral column but no direct invasion to local structures. The exact character could not be determined and the MRI appearances were not typical of an adrenal lesion. It appeared as a retroperitoneal solid lesion with high fatty content on T1 out of phase sequence (Figure 1). Additionally, the superior aspect of the mass was not visualized as the chest was not included in the MRI. Our hospital policy is to perform non-contrast MRI scan in pregnant women initially and if needed, further imaging with contrast scan be performed. Following initial MRI findings, endocrinology input was requested before further imaging was performed.

Her endocrine investigation revealed normal serum aldosterone:renin ratio, normal urinary free cortisol excretion, marginally raised 24-h urinary normetadrenaline and markedly raised urinary dopamine at 14,929 and 22,746 nmol/24 h, and urine-3-methoxytyramine (metabolite of dopamine) at 11,365 µmol/24 h (Table 1). As our centre does not have surgical expertise to manage such complex patients with dopamine-secreting tumour, she was referred to the tertiary centre where specialized endocrine surgery was available. Clinically she was thought to have a dopamine-secreting paraganglioma or pheochromocytoma; therefore, phenoxybenzamine 10 mg twice daily was started as an outpatient and dose adjusted by monitoring BP and side effects. Following multi-disciplinary team (MDT) meeting discussion at the tertiary centre, it was decided to continue the pregnancy until 36 weeks' gestation and arrange investigations and surgical intervention of the tumour during the postpartum period. Hence, further MRI with contrast or positron emission tomography (PET) scan was not arranged until the postpartum period. Both mother and fetus were closely monitored and medical therapy continued until the delivery of a healthy baby at 36 weeks by elective caesarean section.

Clinical progress

Four weeks postpartum, a detailed contrast computed tomography scan revealed a 17 × 10 × 8 cm mass within the retroperitoneum and right chest extending from the level of the T9 to the L2 vertebrae. PET scan showed evidence of a paraganglioma. There was no evidence of

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Figure 1. T1- and T2-weighted MRI images of the tumour.

Table 1. Preoperative and postoperative biochemistry investigation.

Biochemistry results	Preoperative date (22 September 2012)	Preoperative data (27 September 2012)	Postoperative data (25 February 2013)
24-h urine noradrenaline	190 (Ref: 0–3000 nmol/24 h)	243 (Ref: 0–3000 nmol/24 h)	206 (Ref: 0–490 nmol/24 h)
24-h urine adrenaline	<10	<10	13 (Ref: 0–93 nmol/24 h)
24-h urine dopamine	14,929 (Ref: 0–2700 nmol/24 h)	22,746 (Ref: 0–2700 nmol/24 h)	1299 (Ref: 0–3400 nmol/24 h)
24-h urine normetadrenaline		3786 (Ref: 0–3000 nmol/24 h)	1.2 (Ref: 0–3.0 µmol/L)
24-h metadrenaline		612 (Ref: 0–1000 nmol/24 h)	0.4 (Ref: 0–1.7 µmol/L)
24-h urine 3-methoxytyramine		11,365 (Ref: 0–2.3 µmol/24 h)	0.8 (Ref: 0–2.4 µmol/L)
Plasma metanephrine			55 (Ref: 80–510 pmol/L)
Plasma normetanephrine			357 (Ref: 120–1180 pmol/L)

regional lymph node involvement based on preoperative imaging as well as intraoperative findings. The patient underwent thoracotomy to excise the thoraco-abdominal tumour. She made an uneventful recovery and histology confirmed ganglioneuroblastoma with neuroblastic element. Histologically, the lesion was completely excised with no vascular invasion. Her postoperative imaging showed no residual tumour and her plasma and 24-h urinary metanephrines returned to the normal range. At present she is not on any medication and is closely monitored with biochemical testing in the form of monthly 24-h urine metanephrines excretion and three monthly MRI imaging.

Discussion

Ganglioneuroblastomas are mainly tumours of childhood with the vast majority reported in two- to four-year-olds and are rare after the age of 10 years.³ Schipper et al.⁴ reviewed all published cases of ganglioneuroblastomas presenting during adulthood where the noted median age of time of presentation was 39 years (range 21 to 88 years) and half of the adults were female. The final histological diagnosis of our case came as a surprise as it is not only rare in adults but it will also be the first case in pregnancy.

In the case review of 50 adult patients, clinical presentation varied markedly. Some patients were completely asymptomatic whilst others had hypertension or pain related to invasion of important structures by the tumour. Out of the 50 adult cases reviewed, 25 patients had

dopamine and its metabolites (homovanillic acid (HVA) and vanillyl-mandelic acid (VMA)) levels available, of which 12 cases had normal levels, whilst the other 12 cases showed increased urinary values for HVA, VMA or both.^{4,5}

Except for a 24-h history of loin pain, our patient was completely asymptomatic. As she had raised urinary normetadrenaline and markedly raised urinary dopamine and 3-methoxytyramine, the differential diagnosis was either paraganglioma or pheochromocytoma.⁶ These patients are at increased risk of hypertensive crisis and poor pregnancy outcome; therefore, our patient was started on phenoxybenzamine.⁷

In our case, the extent of the tumour could not be identified with certainty on the initial MRI which only imaged the abdomen. From the consensus of tertiary centre MDT meeting, surgical excision was deemed too extensive in the same session as the elective caesarean section; therefore, the decision was taken to perform an elective caesarean section at 36 weeks' gestation followed by detailed imaging with contrast CT and PET scan. This allowed more accurate identification of the tumour and planned surgical approach during the postpartum period.

CT and MR imaging with contrast are useful for defining the morphologic features of neuroblastoma and precisely assessing tumour extent. They also determine tumour extension to the retroperitoneal lymph nodes and liver, around the central vessels, and into the vertebral canal.⁸ Our patient's tumour was large, extending from T9 to L2, although the most common site reported in adults is the abdomen.⁹

Reported literature supports surgical resection of ganglioneuroblastoma in childhood as the treatment of choice. In this age group,

unresectable or disseminated ganglioneuroblastoma responds well to radiotherapy and chemotherapy. However, due to the rarity of tumours in adults, there is no consensus regarding optimum treatment. The literature has not shown any objective improvement in tumour size, recurrence and prognosis with either radiotherapy or chemotherapy. Surgical resection appears to be the only curative regimen, with the option of chemo-radiotherapy when the resection had been incomplete or tumour recurrence is seen.^{4,10} In most cases, the metastases were seen locally and almost half did not show metastases.⁴ The mean survival of adult patients is 13 months with better prognosis noted in those who had complete clearance at surgery.¹⁰

Our patient's prognosis is favourable based on complete tumour resection at surgery, absence of metastasis or infiltration on preoperative imaging studies or during surgery, normalization of urinary metanephrines and histopathological evidence of a well-differentiated tumour. However, we cannot comment on long-term prognosis with certainty as the natural history of these extremely rare tumours is unknown in the adult population.

Conclusion

The rarity of ganglioneuroblastoma, with its occurrence mainly in the paediatric population, makes this an unlikely diagnosis in an adult patient with an adrenal mass. There is virtually no available evidence related to safety of vaginal delivery in this setting. Therefore, it is best practice to manage medically in multi-disciplinary setting until the fetus is viable using the same drug regimen as for regular surgical preparation of cases with pheochromocytoma. Tumour removal during caesarean section is preferred when the tumour is small. However, as our patient was noted to have large tumour on initial abdominal MRI and the tumour was deemed to be extensive requiring thoraco-abdominal approach, elective caesarean section followed by surgical removal during postpartum was considered. Due to the rarity of these tumours in adults, the long-term prognosis cannot be determined with certainty. Therefore, these patients warrant life-long follow-up, as there is potential for recurrence and metastasis.

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Declaration of conflicting interests

None declared.

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Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Guarantor

Dr Manjusha Rathi, the main endocrinology clinician of the patient as the joint obstetric/endocrinology team.

Contributorship

BFC: Drafted and was the main contributor of writing of the manuscript and was the main correspondent and submitted the article for publication. MR: Analysed and interpreted the patient data regarding the ganglioneuroblastoma diagnosis, was the main endocrinology clinician of the patient as the joint obstetric/endocrinology team and revised the manuscript. SAI-S: Interpreted the patient data regarding the ganglioneuroblastoma diagnosis, was the main obstetric clinician of the patient as the joint obstetric/endocrinology team and revised the manuscript. JR: Involved in planning the submission of the manuscript and revised it critically. All authors read and approved the final manuscript.

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