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A case report and the review of the literature

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INTRODUCTION:*Prenatal diagnosis of pheocromocytoma, although rare, is important as it allows a reduction in both maternal mortality and foetal loss. Pheocromocytoma operated on in the first trimester of pregnancy with survival of both patient and foetus is rare in literature. Our case was operated on with success after a correct and early diagnosis was obtained despite a chronic hypertension which existed long before pregnancy. Our case study well illustrates that a correct multidisciplinary approach involving endocrinologists, anesthesiologists, surgeons and gynecologists is fundamental for a positive outcome.*
CASE REPORT: *The case of a white caucasian pregnant woman at 13th weeks of gestation with pheocromocytoma and severe and unstable hypertension that could not be pharmacologically controlled is described. Morphological diagnosis was safely obtained by Magnetic Resonance Imaging (MRI) without intravenous medium contrast agent. Pre-operative treatment consisted of therapy with alpha-blockers and rehydration. Adrenalectomy was performed through a laparotomy. Post-operative treatment consisted of rehydration and ephedrine continued until the fourth post-operative day. The post-operative period was uneventful and a new ultrasound (US) scan confirmed foetal vitality. The patient was discharged seven days after surgery. A live newborn was physiologically delivered after a nine-month pregnancy.*
CONCLUSION: *A correct diagnosis in all pregnant women with severe hypertension particularly those not screened for secondary hypertension and a multidisciplinary management are mandatory to obtain optimal results and avoid deleterious effects at delivery.*

Key words: Adrenalectomy, Hypertension, Pheocromocytoma, Pregnancy.

Introduction

Pheochromocytoma is a rare disease that may occur during pregnancy and is life-threatening for both foetus and mother [1]. Prenatal diagnosis, although rare, is important as it allows a reduction in both maternal mortality and foetal loss [2-3]. In this report we describe the case of a pregnant woman at the 13th week of gestation and analyse the literature to find a correct approach to this critical condition.

Case report

A 30 year old Italian caucasian woman who had suffered from several hypertensive crises after exercise for about one year and had been diagnosed with mild hypertension, came to our attention at the 13th weeks of ges-

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tation, with a diagnosis of pheochromocytoma made by the nephrologists.
At admission, arterial blood pressure values were 180/120 mmHg despite anti-hypertensive therapy with calcium channels blockers and β-blockers. Urinary catecholamines were also elevated. US scan showed a hypoechogenic nodule, of the left adrenal gland about 3 centimeters in diameter of the left adrenal gland. Magnetic Resonance (MRI) imaging, safely obtained without injection of contrast medium, revealed a lesion developing between the left adrenal gland and the kidney, indicative of a neuroendocrine tumor originating from paraaortic ganglionic structures (Fig. 1).
After a careful multidisciplinary (nephrological, anesthesiological and surgical) evaluation, the patient underwent surgery considering the failure of medical treatment to control the hypertension.
Pre-operative treatment consisted of therapy with β-blockers (Doxasosin mesylate 2 mg/day for 5 days) and rehydration (1000 ml saline solution 2 days before surgery and 2000 ml of the same solution the day before surgery). The blood pressure was controlled by pharmacological treatment.
During surgery, a left adrenal mass, about 5,5 x 4 x 2,5 centimeters in size, was found and a total left adrenalectomy was performed through a laparotomic access. US scan immediately after surgery showed a live foetus.
Post-operative treatment consisted of Ephedryn 25 mg, initially infused at a rate of 60 ml/hour for the first five hours, and then 30 ml/hour for ten hours. Rehydration was obtained by a continuous drip of 4000 ml of saline solution and 1000 ml of 5% glucose with the addition of Potassium Chloride (120 mEq). Ephedryn infusion was stopped after the first post-operative day, while hydration was continued until the fourth post-operative day, decreasing the volume from 5000 to 2000 ml/day. The post-operative period was normal uneventful and a new US scan confirmed foetal vitality. The patient was discharged seven days after surgery.
A live newborn was physiologically delivered after a nine-month pregnancy.

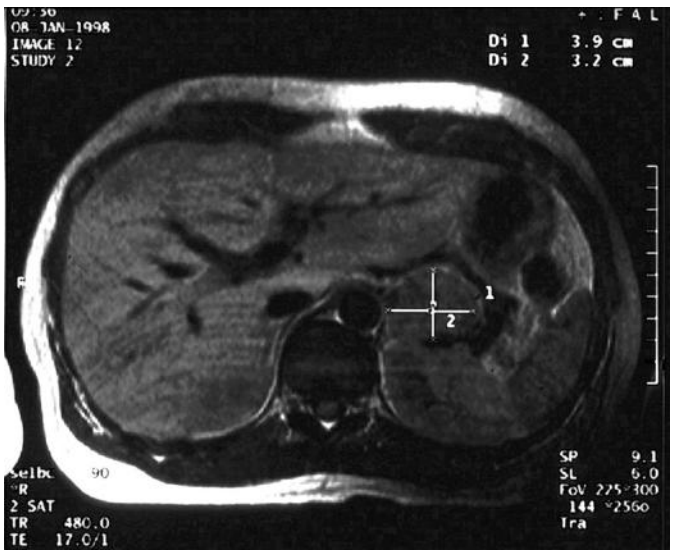

Fig. 1: Spin Echo MRI T1 weighted without contrast agent injection demonstrating a lesion developing between left adrenal gland and kidney, indicative of a neuroendocrine tumor.

Discussion

Pheochromocytoma during pregnancy represents a critical condition and several approaches to it are described in literature [1-2]. Undiagnosed pheochromocytoma is associated with maternal and foetal mortality of up 58% and 56% respectively [4].
Early diagnosis is the main factor influencing prognosis. Mild hypertension is a quite a common finding during pregnancy, hence these patients should be carefully studied at the beginning to exclude the presence of common conditions such as essential hypertension, preeclampsia, and thyrotoxicosis [1,3,5]. Elements differentiating between hypertension and toxaemia in pregnancy are: relative lack of proteinuria (only 23% in these cases), rare appearance of oligo-anuria and thrombocytopenia, hypertension exacerbated while supine [1, 5-6].
Moreover, pregnant women with chronic severe hypertension particularly if associated with paroxistic or postural hypertension and arrhythmias [3] should be screened for pheocromocytoma by 24 hours urine sampling for catecholamines, vanil-mandelic acid and metanephrines. This sampling, on the other hand, may also be requested following the incidental discovery of an adrenal mass during a routine US examination [2], as in the case here described.
The introduction of US scan and MRI imaging allows for early and safe diagnosis of pheocromocytoma [5,3] with a great reduction in both foetal loss and maternal mortality compared to past years: maternal mortality fell from 48% before the 70's to near zero in the 90's, while fetal loss fell to about 15% [4,6-9]. Today MRI is a safe exam and gives most information about the nature and anatomy of the mass without major ionizing radiation exposure. Because intravenous Gadolinium agents do cross the placenta and any effects are not fully understood we preferred avoid its use. Even if some authors consider computer tomography (CT) scan and meta-iodo-benzyl guanidine (MIBG) scintigraphy safe procedures during pregnancy as well [9], we preferred to avoid exposure to ionizing radiations in this case.
Timing of treatment must be decided depending on to how well the hypertension is medically controlled, tumour size, the likelihood of malignancy and stage of pregnancy [6]. The timing of treatment has been widely discussed and numerous approaches described.
During the first two trimesters of pregnancy, some authors suggest removing the tumour as soon as the diagnosis is confirmed [5-6, 9,10] since medical therapy could

become ineffective if delayed for a long time. Other authors suggest, when reasonably possible after 24 weeks gestation, pharmacological control of hypertension until foetal maturity is reached.
In these patients, tumour removal can then be performed along with the caesarean section or 2-3 weeks thereafter [2,5-6,10].
Although many authors sustain that labour and vaginal delivery must be carefully avoided in all cases of pheocromocytoma to prevent acute hypertensive crises, maternal collapse or death [2, 5, 7-8], others [6] consider it possible, especially if the mother is well controlled medically and has had previous, vaginal deliveries.
In the patient here described, hypertension could not be controlled pharmacologically. This was the main indication to perform the adrenalectomy at the 13th week of gestation despite the high-risk of the procedure for both the mother and the foetus. Moreover, MRI showed a mass of 5.5 cm in main diameter whose origin was unclear.
If the diagnosis is made later in pregnancy, pharmacological control of hypertension is suggested to allow for a caesarean section with simultaneous or delayed tumor removal as already described.
Whatever the chosen approach may be, multidisciplinary management of these patients is essential before, during and after the operation [2].
Correct pharmacological preparation prior to surgery is fundamentally important. Different protocols are described in literature to obtain control of hypertension Many authors suggest preparation with phenoxyibenzamine to obtain an β-adrenergic blockade eventually associated withto β-blockers [3,5-6,8] one – two weeks before surgery.
In the case described, the anesthesiologists decided to use phenoxybenzamine after unsuccessful treatment with calcium channel and β-blockers, obtaining complete control of hypertension both before and during surgery. Moreover, the massive post-operative hydration avoided any hypotensive crises that might have proven fatal to the foetus.
Furthermore, all these measures may avoid more serious and deleterious complications such as cardiomyopathy, left ventricular failure or myocardial infarction.
A final consideration is the surgical method by which adrenalectomy is performed. The laparotomic approach was chosen because of the mass location, its dimension that was at the upper limit for laparoscopy at that time when we actually started our experience in adrenal gland laparoscopic surgery and, finally, because we favored the speed of surgery in a pregnant woman. Nevertheless some authors [(6,11-12)] believe the laparoscopic adrenalectomy might favorably impact the outcome for both mother and foetus, since it is associated with less pronounced hemodynamic alterations and lower circulating catecholamine levels. We believe that there is now evidence to propose today the laparoscopic approach also in pregnant women as a safe procedure provided that the surgeon is skilled in the laparoscopic procedures. This conduct is even more evident for functioning masses at the beginning of pregnancy.
However, preoperative diagnosis and multidisciplinary management of these patients are the main factors influencing a favorable outcome for both the foetus and mother.

Conclusion

All young pregnant women with worsening of chronic hypertension diagnosed before the 20th week of gestation should be screened for secondary hypertension in order to obtain an early diagnosis of pheocromocitoma, to avoid deleterious effects on mother and foetus. Modern tools such as US scan and MRI allow early and safe diagnosis during pregnancy.
The timing of surgical treatment has been matter of debate and depends on the stage of pregnancy and the effectiveness of medical therapy in the control of hypertension.
Many authors suggest postponing surgery until the end of gestation or at least until after the 24th week. In any case multidisciplinary management is crucial before, during and after surgery.
Pharmacological preparation with phenossibenzamine and calcium channel blockers and β-blockers associated with massive peri-operative hydration are usually effective in controlling hypertension.

Riassunto

La diagnosi prenatale di feocromocitoma, sebbene rara, è importante dal momento che permette una riduzione della mortalità materna e fetale. Il feocromocitoma operato nel primo trimestre di gravidanza e che comporti la sopravvivenza di madre e figlio è rara in letteratura. Il nostro caso fu operato con successo dopo avere ottenuto una diagnosi precoce corretta malgrado un'ipertensione cronica che pre-esisteva alla gravidanza. Il caso presentato illustra come un corretto approccio che coinvolga endocrinologi, anestesisti, chirurghi e ginecologi sia fondamentale per un buon esito finale.
PRESENTAZIONE DEL CASO: Viene descritto il caso di una donna bianca incinta alla tredicesima settimana di gestazione con un feocromocitoma e una severa e instabile ipertensione non trattabile farmacologicamente. La diagnosi morfologica fu ottenuta mediante una Risonanza Magnetica senza mezzo di contrasto endovenoso. Il trattamento pre-operatorio consistette in β-bloccanti e reidratazione.
La surrenenalectomia fu eseguita mediante laparotomia ed il trattamento postoperatorio consistette in reidratazione ed epinefrina fino alla quarta giornata postopera-

toria. Il decorso postoperatorio fu regolare ed un'ecografia confermò la vitalità del feto. La paziente venne dimessa dopo 7 giorni. Un feto normale fu partorito fisiologicamente al termine del nono mese di gravidanza.

CONCLUSIONI:Una diagnosi etiologica corretta della ipertensione in tutte le donne in gravidanza in particolare in quelle in cui non è stato eseguito uno screening per depistare una ipertensione secondaria ed un trattamento multidisciplinare sono raccomandati per ottenere un risultato ottimale e per evitare effetti deleteri al momento del parto.

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