IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 12 Ver. III (December. 2016), PP 75-77
www.iosrjournals.org

Cushing's Syndrome in Pregnancy: A Report of Three Cases And Literature Review

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Abstract: *Cushing's syndrome is a rare condition. it is much less frequent to diagnosis it during pregnancy. We report the cases of three patients in whom Cushing's syndrome appeared during pregnancy and revealed by hypertension associated with diabetes mellitus and signs of endogenous catabolic. Hormonal balance was in favor of a non- ACTH -dependent hypercortisolism and MRI revealed a unilateral adrenal tumor in the three cases: Adrenocortical carcinoma (n = 2) and adrenal adenoma (n = 1). The evolution was marked by fetal death in utero in three patients. Adrenalectomy is performed for healing in the case of adenoma while for adrenocortical additional treatment with chemotherapy and OPPDDD were indicated. Unfortunately one patient died at the waning of the first course while in the other patient appeared locoregional metastases for which reoperation was performed.*

Keywords: *Cushing's syndrome; pregnancy; Adrenocortical adenoma, adrenocortical carcinoma*

I. Introduction

Cushing's syndrome is rare during pregnancy. Its frequency is estimated at 1 new case per year per million people. In the literature, nearly 125 clinical cases have been reported. The hypercortisolism is responsible for disruption of the menstrual cycle by inhibition of hypothalamic pituitary gonadal axis and a secondary infertility.[1] The positive diagnosis is difficult. Pathology cannot be recognized because of signs that may be associated with pregnancy which could compromise fetal and maternai prognosis and lead to severe complications. Indeed, maternai and fetal mortality are reported in 5% to 25 %.[2,3] 2 of 3 pregnancies are complicated and fetal and maternal prognosis is severely compromised.[2] Adrenal causes are dominant. An imaging must be performed quickly to eliminate an adrenocortical carcinoma and undertake an effective treatment.[3] We report three cases in this regard.

II. Observations

Three patients aged of 38 years (Patient AM) ; 34 years (Patient DS) and 28 years (Patient BN) were hospitalized in our department for evaluation of Cushing's syndrome associated with ongoing pregnancy of 28, 30 and 18 weeks of amenorrhea. Cushing's syndrome was diagnosed after the onset of hypertension and diabetes mellitus in a context of excessive weight gain and appearance of important stretch marks. Physical examination on admission found signs of hypercatabolism , without mélanodermia or signs or abdominal tumor or brain (Fig 1). Hypertension and diabetes mellitus occurred at 10 weeks of gestation in AM, 12 in DS and 9 in BN have not alarmed gynecologists and it is only at the exacerbation of symptoms and the appearance of a frank evocative table, that they are oriented in endocrinology. The abdominopelvic ultrasound imaging and magnetic resonance imaging revealed the presence of an adrenal mass in three patients. It was heterogeneous, with fuzzy and large size limits in two cases respectively 13cm (patient AM) and 16 cm (patient DS)(Fig2) while the third patient (BN) had a homogeneous and well rounded mass of 40 mm. Hormonal results showed elevated plasma blood cortisol with a circadian cycle out of and a collapse rate of ACTH (Table I). Urinary and salivary free cortisols were not performed as well as the braking tests.

The urinary methoxylated derivatives were high in patients AM and DS. Symptomatic treatment is undertaken in three patients. Unfortunately the severity of hypertension resulted in fetal death in the three cases. Adrenalectomy is performed soon after leading to the healing of the patient BN, while in the other two, additional chemotherapy and OPDD was indicated. Indeed, histological study was in favor of a benin adenoma on BN and an adrenocortical carcinoma in the patients AM and DS. Unfortunately, evolution was rapidly unfavorable marked by the death of AM at the waning of her first course in an array of secondary generalized metastasis and recurrence in DS with the appearance of a pancreatic metastasis for which reoperation was decided. The penny stock of impact has revealed pulmonary locations. Secondary locations had appeared less than six months after the diagnosis in the two patients.

III. Discussion

Both positive and etiological diagnoses of Cushing's syndrome are difficult in pregnancy. Clinical signs are nonspecific and may be mistakenly considered by parties' complicated pregnancy as excessive weight gain, gestational hypertension or gestational diabetes.[4,5] Biologically, physiological changes in cortisol caused by pregnancy are important and should be recognized. Rising CLU must be interpreted cautiously due to a physiological increase in the production of cortisol particularly during the 2nd and 3rd quarter. Similarly, dexamethasone freination is reduced during pregnancy, which can cause false positive particularly for minute braking test. The diagnosis then rests essentially on the abolition of circadian cortisol.[3,6] The biological hyperandrogenism usually observed is not discriminatory however the magnitude of this increase should be carefully interpreted.[7] The management of a patient with hypercortisolism with ongoing pregnancy requires identifying the origin hormone production and provide appropriate therapy. When the cause of hypercortisolism is an adrenocortical adenoma, the therapeutic indication is adrenalectomy during pregnancy or medical treatment followed by surgery after delivery. [8] When surgery is indicated during pregnancy , it should preferably be carried out during the second quarter to minimize maternal-fetal morbidity.[9,10] During the third quarter, the therapeutic management should be symptomatic and delivery scheduled as early as possible.

Adrenocortical carcinoma is rare and its occurrence during pregnancy is not reported. This is a very unfortunate tumor prognosis with a survival rate of <30 % at 5 years.[2,3] Several studies have demonstrated a close relationship between the female and adrenocortical carcinoma. Indeed adrenocortical carcinoma is more common in women with a sex ratio of 4.2.[12] The adrenal benign and malignant tumors are responsible for the majority of causes of hypercortisolism during pregnancy while they are much less common outside of pregnancy.[13]

Adrenocortical carcinoma associated with pregnancy is diagnosed at a more advanced than non-pregnant patient stage. The tumor is larger and is rapidly progressive[14]. Furthermore molecular studies have demonstrated an abnormal increase in the secretion of the IGF2 as observed in the fetal adrenal and expression of estrogen receptor and progesterone at rates as high as see in breast neoplasia.[3,15] Also, Hormonal inflation that characterizes pregnancy is responsible for a severe scalability tumor where more reserved prognosis of patients in this case.[16] As in all cases of adrenocortical carcinoma associated with pregnancy, fetal prognosis is compromise. The fetus may suffer from intrauterine growth retardation, prematurity, perinatal or intrauterine mortality.[17,18] The prognosis of patients can be improved if hypercortisolism treatment is initiated early in the course of pregnancy. Unfortunately, the diagnosis is often made late and morbidity is high.[13] The treatment of the cause of hypercortisolism should be undertaken whenever is possible. Experience with anti hypercortisoliques drug is very limited. They are considered only in case of severe hypercortisolism and if against surgery indication. The métopyrone, and ketoconazole have been used with success and no adverse effects were found.

The aminoglutitimide causes fetal masculinization where it's against his indication in pregnancy. When the diagnosis of tumor or corticossurénalien adenoma is made, surgery should be considered. In fact, there's no consensus in the therapeutic management. The optimal time for adrenalectomy is the second quarter in order to not compromise the fetal-maternal prognosis. In the third quarter, conservative treatment is preferred and surgery is performed after programming a premature birth. To avoid fetal manipulation and hypertension caused by laparoscopic techniques, laparotomy is preferred.[19] In case of adrenocortical evolutionary stage 3 and 4 or complicated secondary metastasis, medical abortion should be considered.

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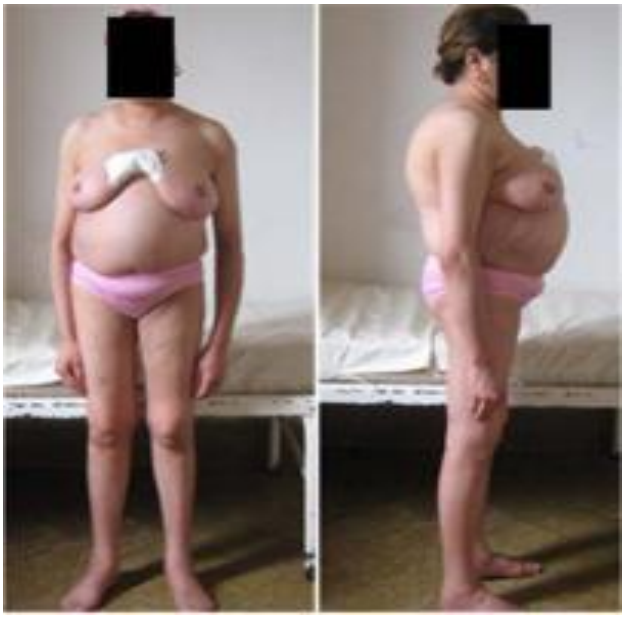

Fig 1: Cushing's syndrome in a pregnant patient

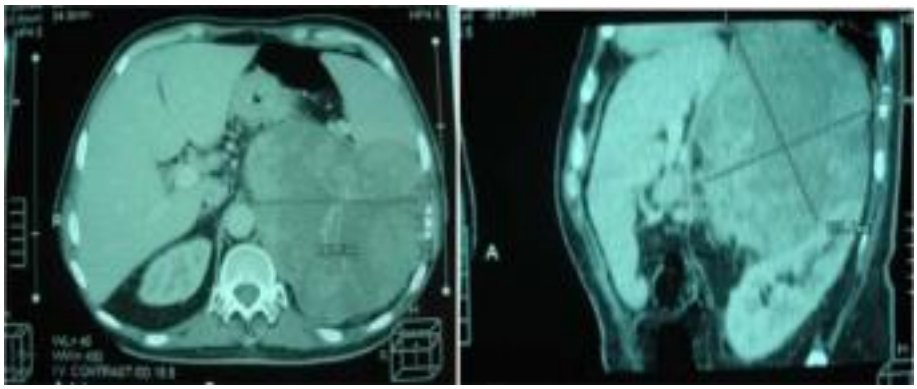

Fig2: Voluminous Adrenocortical carcinoma