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Case Report

A CASE REPORT OF INFLUENCE OF FREE TYROSINE KINASE/ PLACENTAL GROWTH FACTOR (SFLT-1/PLGF) RATIO TEST FOR PREECLAMPSIA ON CLINICAL DECISION MAKING IN SCREENING POSITIVE WOMEN

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Summary

Preeclampsia (PE) is characterized by hypertension and proteinuria after the 20th gestational week (GW). It is a significant cause of maternal and fetal perinatal morbidity and mortality during pregnancy. There is increasing evidence suggesting that PE is due to an impaired balance between maternal placental angiogenic and antiangiogenic factors that harm maternal vascular endothelium. The study aimed to assess the clinical and financial aspects of introducing into practice the soluble fms-like tyrosine kinase (sFlt-1) to placental growth factor (PlGF) ratio test to improve the management of preeclampsia and adverse pregnancy outcome, intrauterine growth retardation, iatrogenic prematurity, and placental abruption.
We report a case study in which we used the sFlt-1/PlGF ratio in the management of a high-risk pregnancy. Unnecessary hospitalization was avoided, and the patient was managed appropriately.
Key words: preeclampsia, sFlt-1/PlGF ratio, adverse pregnancy outcome

Introduction

Preeclampsia (PE) is characterized by hypertension and proteinuria after the 20th gestational week (GW) and is a major cause of maternal, perinatal morbidity, and mortality during pregnancy [1]. The incidence on a global scale is subject to discussions, but it has been accepted in the last years that it affects between 2 and 8% of all pregnancies [2]. Forty-two percent of all maternal preterm deliveries are correlated to PE [2]. According to Shennan et al., sub-standard care accounts for 20 out of 22 lethal outcomes, which are associated with preeclampsia, and 63% were defined as undoubtedly avoidable [3]. PE was divided into early - before the 34th gestational week, and late - after the 34th gestational week [1].

During the last several decades, most of the efforts of exploratory groups were directed to the clarification of the etiology and pathogenesis of preeclampsia, discovery, and application of different preventive and therapeutic means for treatment. The pathogenesis of PE is still not well understood, regardless of the enormous number of researches [2]. It is clear that the condition

originates from the placenta, and its target is the maternal endothelium [4, 5]. We present a case of a 30-year-old tertiparous woman at high-risk for developing severe preeclampsia, in which we used the sFlt-1/PlGF ratio for the optimal management of the pregnancy.

Case description

We present a 30-year-old patient with a third pregnancy and second parturition. She did not report any concomitant diseases. She was overweight with a body mass index 29. Her first pregnancy five years ago ended with the parturition of a dead hypotrophic fetus with a bodyweight of 2000 grams (g), in the 38th (+2) gestation week. At the moment of parturition, her blood pressure raised to 180/110 mm Hg, and proteinuria of 0.6 g/l was found. Paraclinical parameters and blood pressure had not been followed during pregnancy.

Highly increased resistance of blood flow in the uterine arteries was found during her second pregnancy, assessed by the pulsatility index, with the presence of bilateral notching bilaterally on Doppler ultrasound, on a visit for antenatal assessment of the fetal morphology in the second trimester (20th gestational week). After that, the patient visited the Department of Pregnancy Pathology every month for evaluation of her status and the condition of the fetus. Her blood pressure reached nearly 150/100 mm Hg since the 29th gestational week and proteinuria of up to 0.3 g/l. Antihypertensive medication was prescribed. Correction of hypoalbuminemia was performed at the time of parturition. Blood pressure of up to 170/110 mm Hg was found. The patient delivered a live fetus with a bodyweight of 2900 g in 38th (+0) gestational week.

She was pregnant in 20th (+1) gestational week at the time of her first visit to our clinic for evaluation of fetal anatomy in the second trimester. The blood pressure at this moment was normal. One eutrophic fetus of female gender was found on examination, with normal fetal anatomy. On Doppler examination of the uterine arteries, highly increased resistance was found bilaterally, with the presence of notching on the right side uterine artery pulsatility index (UTPI) – 1.68, uterine artery resistance index (UTRI) – 0.83; on the left side UTPI – 2.4, UTRI – 0.74; with bilateral notching. The patient was followed up on an out-patient basis, and her blood pressure was checked. Test strips were used for checking proteinuria. The sFlt-1, PlGF, and sFlt-1/PlGF ratios were examined twice during the pregnancy by immunological test for in vitro quantification of (sFlt-1) and PlGF in human serum. The first sample was taken in the second trimester (22nd GW), and the second sample was taken at the beginning of the third trimester of the pregnancy (28th GW). The two results were below the considered cut-off value of 38. (Table 1).

She was not hospitalized during this pregnancy until going into labor. The pregnancy ended with the parturition of a live fetus with a bodyweight of 3130 g in 39th (+0) gestational week. The blood pressure was within the normal range. The urinary test was normal.

Discussion

Hypertensive abnormalities during pregnancy are the third leading cause of maternal mortality after hemorrhage and infectious complications. Placental dysfunction and the associated complications account for 18% of the lethal outcomes of parturient women in the world. The incidence of PE on a global scale is a subject of discussions, but in the last few years, it is estimated to affect between 2 and 8% of all pregnancies [2]. Despite its major social significance, an explicitly accepted screening model for early diagnostics and identification of these patients still does not exist. The management of PE is also associated with significant health care costs [6, 7].

Several markers were studied for

Table 1. Results of studied biomarkers in two stages of pregnancy

	22nd (+1) gestational week	**28th (+1) gestational week**
sFlt-1	1040 pg/ml	1543 pg/ml
PlGF	97.87 pg/ml	339.7 pg/ml
sFlt-1/PlGF ratio	10.63 ratio	4.54 ratio

determination of their role for calculating the risk for development of PE, for introduction in combined screening and improvement of its predictive value. The first biophysical marker used in the predictive screening model is the average blood pressure. Poon et al. found that the combined screening model in the first trimester, using the average blood pressure and maternal medical history, identified successfully about 60% of patients, who had PE several months after the time of examination, and about 40% of those who had gestational hypertension with 10% false positive frequency.

Since it is now clear that PE represents a form of placental dysfunction, attempts are undertaken for introducing the sFlt-1/PlGF ratio in the prediction, diagnosis, and prognosis for PE development. The ratio of sFlt-1/PlGF can become a fundamental tool in overcoming of preeclampsia, especially as an automatic test, which allows for rapid and easy measurement of these markers [8]. The ratio of serum fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) has diagnostic value, and this ratio forms the basis of the first automated biomarker test for preeclampsia, the Elecsys® sFlt-1/PlGF immunoassay ratio (Roche Diagnostics GmbH, Mannheim, Germany) [9, 10].

Having in mind the obstetrical medical history for two previous pregnancies with preeclampsia, and highly increased resistance in the uterine arteries, our patient was highly suspected for developing PE and adverse outcome of the pregnancy. That is why, during the previous pregnancy, the woman was hospitalized monthly at the Department of Pregnancy Pathology for assessment. This approach, however, was quite economically non-effective. During the current pregnancy, a decision was made for the assessment and management of the patient by using sFlt-1/PlGF immunoassay ratio during the second trimester of pregnancy. Based on the results from the ratio, the values of which were below the cut-off value of <38 [11], the patient was observed on an out-patient basis. The pregnancy outcome was normal.

Conclusions

We used the sFlt-1/PlGF ratio test into clinical practice to manage high risk for severe PE. Based on the low rates of the ratio measured twice during the second trimester of pregnancy, we managed the pregnancy appropriately without unnecessary hospitalization. Further studies are necessary for the assessment of the possibilities of sFlt-1/PlGF ratio test in the prediction, diagnosis, and prognosis of preeclampsia.

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