

Expression of Human Chorionic Gonadotropin (β hCG) in Pre-eclamptic Placenta

Expresión de Gonadotropina Coriónica Humana (β hCG) en Placenta Preecláptica

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SUMMARY: This study aimed to assess association between preeclampsia with trophoblast cells and serum level of b-human chorionic gonadotropin (β -hCG). Were compared 20 patients with preeclampsia and 20 control patients with respect to demographics, hematological parameters and the presence of trophoblast in placental samples. Patchy necrosis with loss of microvilli and gross thinning of the syncytium with distorted microvilli were seen in terminal villi of placentae of women with pre-eclampsia Syncytial cells at the molecular level crossings, especially at the level of β hCG in conjunction with the changes in the preeclampsia was made on the histopathological changes to clarify the villi.

KEY WORDS: Pre-eclampsia; Placenta; β hCG; Syncytiotrophoblast.

INTRODUCTION

Preeclampsia is a transient disorder which develops during last trimester of pregnancy or immediately after delivery and affects 3-8% of all pregnant women (Redman & Sargent, 2005; Duley, 2009). Appropriate organization of the placenta involves the differentiation of cytotrophoblasts into multinuclear syncytiotrophoblast or extravillous trophoblasts. Extravillous trophoblasts play a crucial role in the establishment of utero-placental circulation (Strickland & Richards, 1992; Cross *et al.*, 1994). Researchers note the effects of trophoblast cells in the pathogenesis of preeclampsia found in trophoblast cell migration and placenta planting regulatory mechanisms play an important role. Although the synthesis and secretion of hCG by the villous trophoblast is well established and documented, presence of hCG in the cytotrophoblast from extravillous origin remains controversial since opposite results were reported by different authors (Gosseye & Fox, 1984; Kurman *et al.*, 1984; Sasagawa *et al.*, 1987).

MATERIAL AND METHOD

Placenta materials were obtained from patients who gave birth in hospital obstetrics. In addition, as a control

group, human placental tissues from 20 normotensive pregnancies was collected from severe preeclamptic women at 24-38 (20 placentas) weeks of gestation. New onset hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) and proteinuria (>300 mg in 24 h) was observed in all the patients included in preeclampsia group. Immediately after delivery, the placental tissue was transported from the delivery room to the laboratory. After preliminary gross examination, tissue samples were obtained from the fetal side of the placenta (1X1X1cm). The specimens were immersed in 10% buffered formaldehyde. Then, 4-6 mm sections were cut and made into slides. These were processed for Trichrom Masson staining, carried out according to conventional procedures.

Immunohistochemical technique. Sections (4-6 μ m thick) were deparaffinized, dehydrated and kept in buffer solution. Heat-induced antigen retrieval in citrate buffer was used for β hCG immunostaining. Slides were blocked with normal serum, incubated with the primary antibodies (used at final dilutions indicated below) for 2 h at room temperature and then with biotinylated secondary antibodies. Detection was based on the labeled streptavidinbiotin complex technique (LSAB kit, DAKO, Glostrup, Denmark), using 3,3'-diaminobenzidine (DAB) as chromogenic substrate.

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RESULTS

In control group placentas, villous structures appeared with connective tissues core covered by trophoblastic cell layers (syncytiotrophoblast and cytotrophoblast cells), each villous was rich with fetal capillaries. Specific histopathologic changes were seen in the preeclamptic placentas. Hyperplasia in the syncytiotrophoblasts, especially the syncytial layer develops sprouts protruding into the intervillous spaces. Also in the field intervillous fibrinoid deposition, syncytial nodes and an increase was observed in the fetal capillaries

Chorionic villous maturation, vascular dilatation and progression of villous congestion were also increased in the connective tissue

In all sections the syncytiotrophoblast shows an intensity of hCG immunostaining higher than the one observed in placentas from normotensive pregnancies. Syncytial sprouts showed intense β hCG expression. Staining for β hCG was prominent in vesicles separating from syncytiotrophoblast into the intervillous space.

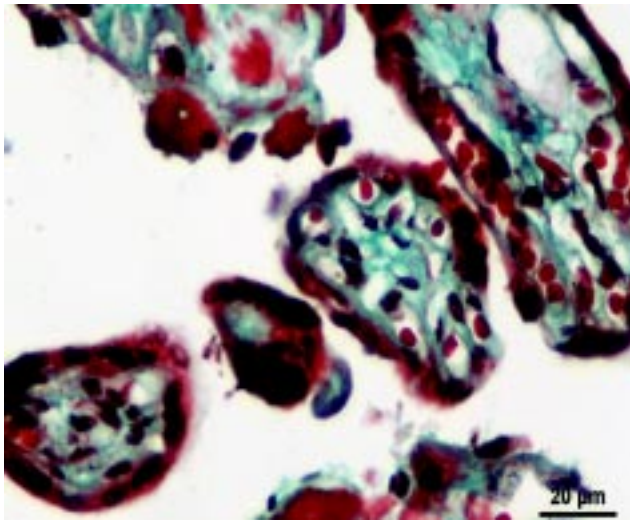


Fig. 1. Control group: the normal appearance of chorionic villi, Trichrom-masson, Bar 20 μ m.

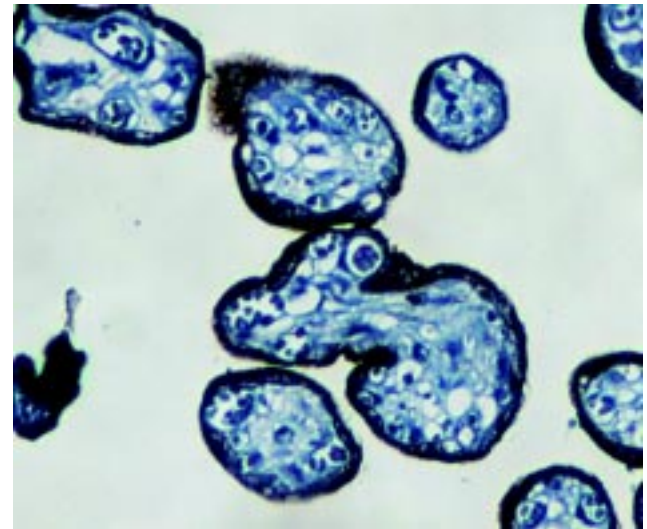


Fig. 3. Control group (a) (β hCG immunoreactivity). Immunocytochemical localization of β hCG in normotensive.

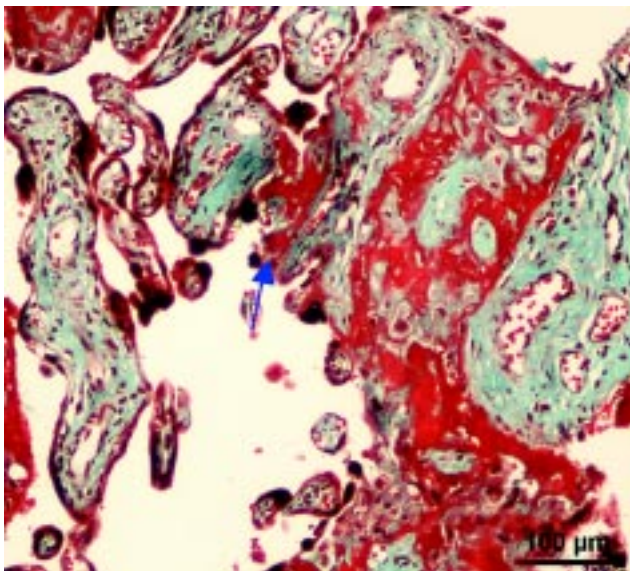


Fig. 2. Fibrinoid necrosis and a increase fibrous tissue (Arrow), dilatation in capillary vessel, a increase syncytial nodes, Trichrom-masson, Bar 100 μ m.

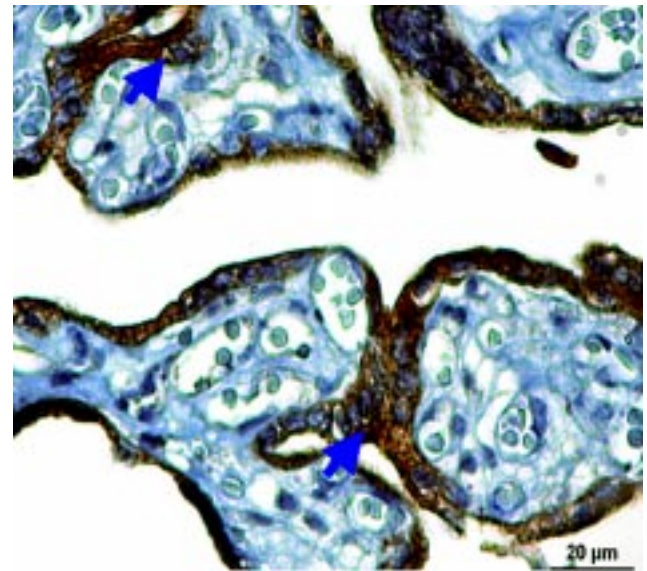


Fig. 4. Pre-eclamptic group β hCG expression in Syncytial cells and Syncytial sprouts and cytotrophoblast (arrow).

DISCUSSION

Preeclampsia has been described as a placental disorder resulting in widespread endothelial dysfunction in multiple vascular beds, abnormal trophoblast invasion thereby causing the characteristic signs and symptoms of Preeclampsia. Several biomarkers and clinical characteristics have been evaluated as predictors of preeclampsia. Several studies have demonstrated an association between elevated second trimester maternal β -HCG and later development of Preeclampsia (Muller *et al.*, 1996; Luckas *et al.*, 1998; Walton *et al.*, 1999).

Recently the concentrations of hCG-h in first trimester serum were found to be lower in mothers who later develop preeclampsia than in controls (Keikkala *et al.*, 2013). β -hCG are commonly used as markers of syncytiotrophoblast (Butler *et al.*, 2009). Serum levels of β -hCG are also elevated in second and third trimester in cases suffering from preeclampsia compared to controls, while in first trimester serum β -hCG is not significantly altered between both groups (Spencer *et al.*, 2008). This study seems to demonstrate that increased production of hCG by preeclamptic placentas is associated with strong hCG immunostaining of the

trophoblast and syncytial knot. In pre eclampsia the cytotrophoblast transformed into syncytiotrophoblast. Human placenta synthesizes steroid, protein, and glycoprotein hormones throughout gestation (Shima & Mailhos, 2000). Gokdeniz *et al.* (2000) found a strict relationship between severe pre-eclampsia and elevated serum b-hCG levels, indicating that there should be an abnormal placental secretory function in patients with severe pre-eclampsia.

Preeclampsia group, serum β -hCG in the syncytiotrophoblast and cytotrophoblast of the increase in expression was found to be more than in normal placenta. β -hCG illustrates the tight association with preeclampsia. It is generally accepted that hCG, are only secreted by syncytiotrophoblasts. In this study, β -hCG are predominantly produced by syncytiotrophoblast and they can be also detected in the differentiating cytotrophoblast. As preeclampsia is probably a trophoblastic disorder, elevated b-hCG is thought to reflect early placental damage or dysfunction. Our results showed that β -hCG may be a good indicator for severe preeclampsia.

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RESUMEN: El objetivo fue evaluar la asociación entre la preeclampsia con células trofoblásticas y concentración sérica de la gonadotropina coriónica humana b (β -hCG). Se compararon 20 pacientes con preeclampsia y 20 pacientes de control con respecto a datos demográficos, parámetros hematológicos y la presencia de trofoblasto en muestras de placenta. Se observaron áreas dispersadas de necrosis, con pérdida de microvellosidades y adelgazamiento del sincitio con microvellosidades distorsionadas en las vellosidades terminales de placentas en mujeres con células sincitiales preeclámpticas a nivel molecular, junto a altos niveles de β hCG asociados a los cambios generados por la preeclampsia sobre los parámetros histopatológicos.

PALABRAS CLAVE: Preeclampsia; Placenta; β hCG; Sincitiotrofoblasto.

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