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Original article

Characterization of apoptosis and autophagy through Bcl-2 and Beclin-1 immunoexpression in gestational trophoblastic disease

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Abstract

Background: The pathogenesis of Gestational Trophoblastic Disease (GTD) is not clearly known.

Objective: In this study, immunoexpression of proteins Bcl-2 and Beclin-1 in trophoblastic lesions and normal trophoblastic tissue was conducted to study the mechanism of apoptotic and autophagic cell death that is expected to complete the study of GTD pathogenesis.

Materials and Methods: Bcl-2 and Beclin-1 immunoexpression were studied on complete hydatidiform mole, partial hydatidiform mole, invasive mole, choriocarcinoma and normal placenta slides.

Results: The average total scores of Bcl-2 immunoexpression had a decreasing value, starting from partial hydatidiform mole (3.09), complete hydatidiform mole (2.36), invasive mole (1.18) to choriocarcinoma (0) when compared to normal placenta (6). The results showed no significant difference in Beclin-1 immunoexpression total score between complete hydatidiform mole, partial hydatidiform mole and invasive mole, namely that the value of the average total score of Beclin-1 was low (2.27, 2.45 and 2.36), but on the contrary choriocarcinoma showed an increasing strong Beclin-1 expression with the average total score of 4.57.

Conclusion: Bcl-2 expression decreases in line with the excessive proliferation of trophoblast cells in hydatidiform mole and leads to malignancy in invasive mole and choriocarcinoma. The decreased expression of Beclin-1 that leads to autophagy defects in complete hydatidiform mole, partial hydatidiform mole and invasive mole shows the role of autophagy as tumor suppressor, whereas strong Beclin-1 expression shows the survival role of autophagy in choriocarcinoma. The change of Bcl-2 activity as antiapoptosis and Beclin-1 as proautophagy plays a role in pathogenesis of GTD.

***Key words**: Gestational trophoblastic disease, Apoptosis, Autophagy, Bcl-2, Beclin-1.*

This article extracted from Ph.D. thesis. (Teresa Liliana Wargasetia)

Introduction

Benign hydatidiform moles and malignant gestational trophoblastic tumors are included in a group (spectrum) of diseases, namely gestational trophoblastic diseases (GTD). Hydatidiform mole consists of two types, namely complete hydatidiform mole and partial hydatidiform mole, whereas gestational trophoblastic tumor (GTT) is classified into invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor based on anatomic pathology examination (1, 2).

In developed countries, the incidence of hydatidiform mole and GTT is low. The diseases are more common in Asian and Latin-American countries. One of the problems in GTD is that most of the hydatidiform mole will undergo spontaneous regression after curettage, but 8-30% of patients suffer from GTT in the future and need chemotherapy. Until now the prognostic factor used has been the serial assay β-human chorionic gonadotropin (β-HCG) level of the serum measured during follow-up after evacuation. There are no available genetic or other molecular markers to predict as early as possible the aggressive behavior of hydatidiform mole (3, 4).

This research is aimed to study the pathogenesis of GTD by highlighting the mechanisms of programmed cell death. Nowadays, programmed cell death is a field