Expression of Epidermal Growth Factor Receptor (Egfr) in Mole Hydatidiforms, Exaggarated Placental Sites and Normal Placentas and Ki 67 in Mole Hydatidiforms and Normal Placentas 1*

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OBJECTIVE: The aim of this study is to find out differences between expression of EGFR (epidermal growth factor receptor) and Ki 67 labeling index (LI) in complete, incomplete mole hydatidiforms, exaggareted placental sites and normal placentas.
STUDY DESIGN: Eighteen incomplete, 7 complete hydatidiform moles, 19 exaggareted placental sites and 10 placentas (control group) were studied immunohistochemically for EGFR (epidermal growth factor receptor)and Ki 67.
RESULTS: Ki 67 LI of villous cytotrophoblasts differed significantly between complete and incomplete hydatidiform moles ($p < 0.01$). Ki67 LIs of hydatidiform moles were significantly higher than control group ($p < 0.001$). EGFR (epidermal growth factor receptor)staining of villous cytotrophoblasts differed significantly between complete, incomplete hydatidiform moles and control group ($p < 0.001$). EGFR (epidermal growth factor receptor) expression of syncytiotrophoblast differed significantly between complete, incomplete hydatidiform moles and control group ($p < 0.001$).
CONCLUSION: Expression of EGFR (epidermal growth factor receptor)in syncytiotrophoblast and cytotrophoblasts is important in the pathogenesis of complete and incomplete hydatidiform moles. Ki67 LI can be a useful marker in differentiating complete and incomplete moles.
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Key Words: Mole hydatiform, Exaggerated placental site, Ki67 labeling index, EGFR (epidermal growth factor receptor)

The aim of this study is to find out differences between expression of EGFR (epidermal growth factor receptor) in complete, incomplete mole hydatidiforms, exaggareted placental sites and Ki 67 labeling index (LI) in complete, incomplete mole hydatidiforms and normal placentas (2. and 3. trimester).

Material and Methods

Parafin embedded sections of 18 incomplete, 7 complete hydatidiform moles, 19 exaggareted placental sites and 10 placentas (control group), diagnosed previously between 2000- 2004 in the Department of Pathology, School of Medicine, Akdeniz University, Antalya, Turkey, were studied immunohistochemically for EGFR (epidermal growth factor receptor) (DAKO, Clone H11) and Ki 67(Neomarkers, RM-9106-5). Statistical analysis of the results were made using student t or ANOVA with post huc Tukey test.

Formalin fixed, paraffin -embedded tissues were cut 4 -µm- thick sections for immunohistochemical studies.

Results

Staining for Ki 67 was detected immunohistochemically in villous cytotrophoblasts and extravillous intermediate trophoblast of complete, incomplete hydatidiform moles, and only in villous cytotrophoblasts of control group (Figure 1,2). Ki67 LI of villous cytotrophoblasts differed significantly between complete and incomplete hydatidiform moles ($p< 0.01$). Ki67 LIs of hydatidiform moles were significantly higher than control group ($p< 0.001$).

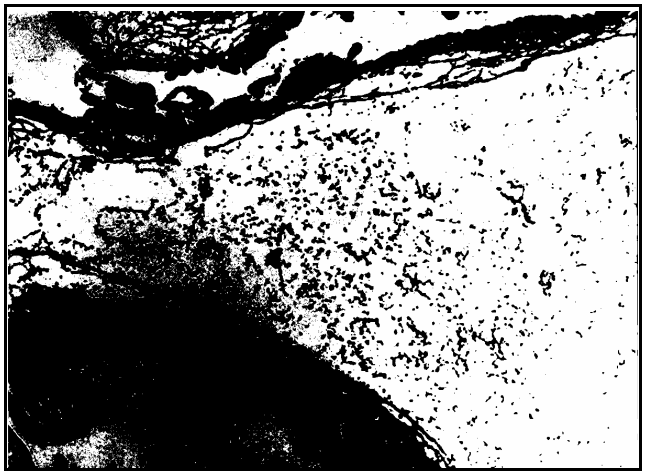

Figure 1. Ki 67 staining in incomplete hydatidiform moles X 200

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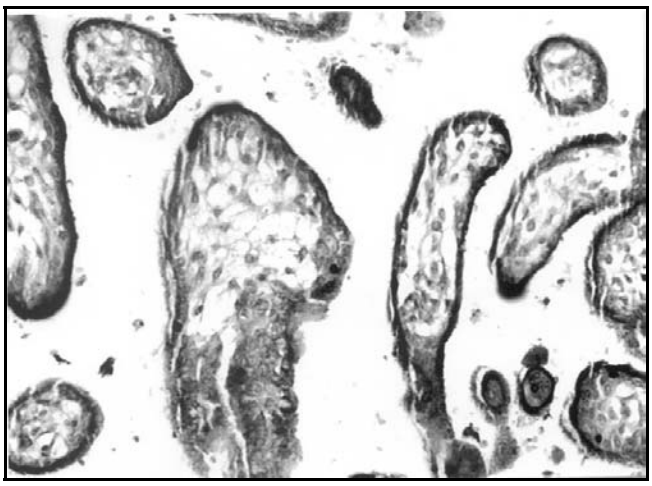

Figure 2. Ki67 staining in complete hydatidiform moles X400

Immunostaining of Ki67 in extravillous intermediate trophoblasts were not different between complete and incomplete hydatidiform moles (p=0.58).

EGFR (epidermal growth factor receptor) was detected in syncytiotrophoblast and cytotrophoblasts of complete and incomplete hydatidiform moles and control group (Figure 3,4). Staining of villous cytotrophoblasts differed significantly between complete hydatidiform moles and control group ($p< 0.001$) and incomplete hydatidiform moles and control group ($p< 0.001$) but staining of villous cytotrophoblasts was not differed significantly between complete and incomplete hydatidiform moles (p=0.10).

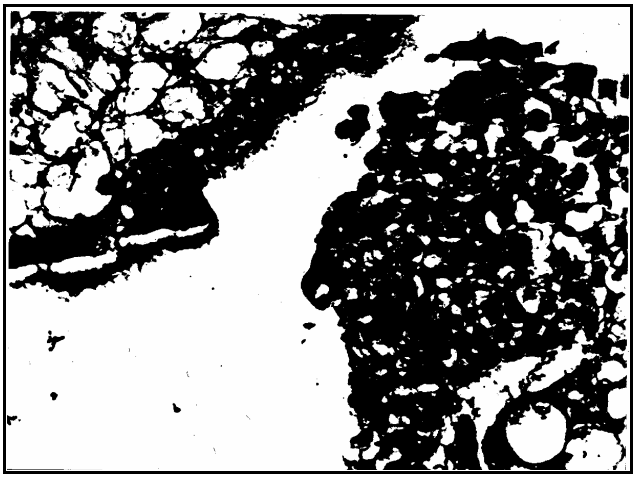

Figure 3. EGFR (epidermal growth factor receptor) staining in complete hydatidiform moles X50

EGFR (epidermal growth factor receptor) expression of syncytiotrophoblast differed significantly between complete, incomplete hydatidiform moles and control group ($p< 0.001$).However the difference of syncytiotiotrophoblasts immunopositivity between complete and incomplete moles was not significant ($p> 0.05$).

EGFR (epidermal growth factor receptor) immunostaining was not detected either in extravillous intermediate trophoblasts of mole hydatidiformes or exaggarated placental site.

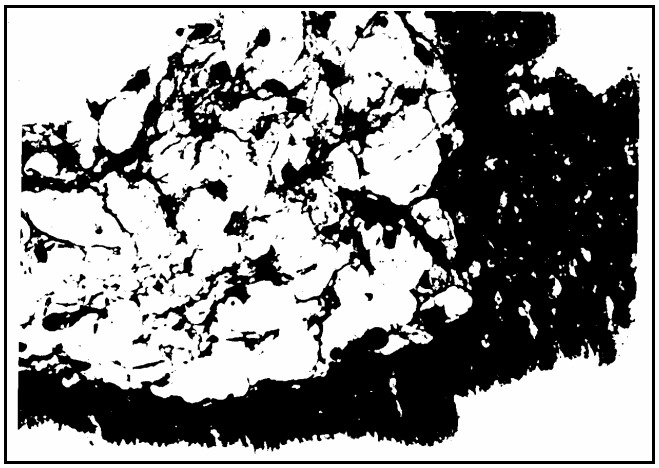

Figure 4. EGFR (epidermal growth factor receptor) staining in normal placenta X50

Conclusion

Mole hydatidiform is an abnormal placenta with villous hydrops and variable degrees of trophoblastic proliferation. It can be separated as complete, incomplete and invasive hydatidiform moles.[1] Most of the malign trophoblastic tumors arise from complete hydatidiform moles; because of this it is very important to separate them. In our study, Ki67 LI of villous cytotrophoblasts differed significantly between complete and incomplete hydatidiform moles ($p< 0.01$). Ki67 LIs of hydatidiform moles were significantly higher than control group ($p< 0.001$).

Immunostaining of Ki67 in extravillous intermediate trophoblasts were not different between complete and incomplete hydatidiform moles (p=0.58). Ostrzega N. et al. also found difference of staining between complete and incomplete hydatidiform moles and abortus with hydrophic changes were statistically significant.[2]

Schammell D.P. et al. found that villous trophoblast nuclei reactive for Ki67 differed significantly between moles and non-moles.[3] Cheung et al. found that Ki67 index in hydrophic abortion, although lower than that for normal first trimester placentas, was much higher than that for term placentas.[4]

Olvera M. et al. showed Ki67 trophoblast staining decreased with increasing gestational age of the placenta, and showed maximal expression in gestational trophoblastic disease.[5]

Kale A. et al. noted significant higher Ki67 expression in gestational trophoblastic disease.[6]

The result of this study showed that Ki67 LI can be a useful marker in differentiating complete and incomplete moles.

EGFR (epidermal growth factor receptor) staining of villous cytotrophoblasts differed significantly between complete hydatidiform moles and control group ($p < 0.001$) and incomplete hydatidiform moles and control group ($p < 0.001$) but staining of villous cytotrophoblasts was not differed significantly between complete and incomplete hydatidiform moles ($p=0.10$).

EGFR (epidermal growth factor receptor) expression of syncytiotrophoblast differed significantly between complete, incomplete hydatidiform moles and control group ($p< 0.001$). However the difference of syncytiotrophoblasts immunopositivity between complete and incomplete moles was not significant ($p> 0.05$).

Tuncer Z.S. et al. observed that expression of EGFR (epidermal growth factor receptor) in syncytiotrophoblasts and cytotrophoblasts of complete mole was significantly greater than the expression of EGFR (epidermal growth factor receptor) syncytiotrophoblasts and cytotrophoblasts of placenta and partial mole.[7]

Ladines-Llave C.A. et al. observed a decrease in EGFR (epidermal growth factor receptor) expression during malignant transformation of trophoblasts in their study with complete hydatidiform moles, invasive hydatidiform moles and choriocarcinoma.[8]

Expression of EGFR (epidermal growth factor receptor) in syncytiotrophoblast and cytotrophoblasts is important in the pathogenesis of complete and incomplete hydatidiform moles.

Negative staining of EGFR (epidermal growth factor receptor) in exaggareted placental sites may show us that EGFR-releated family of oncogens does not play a role in the pathogenesis of exaggarated placental site.

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