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Immunohistochemistry

Evaluation of Hydropic Placentas

(Hydropic Degeneration vs. Partial Mole vs. Complete Mole)

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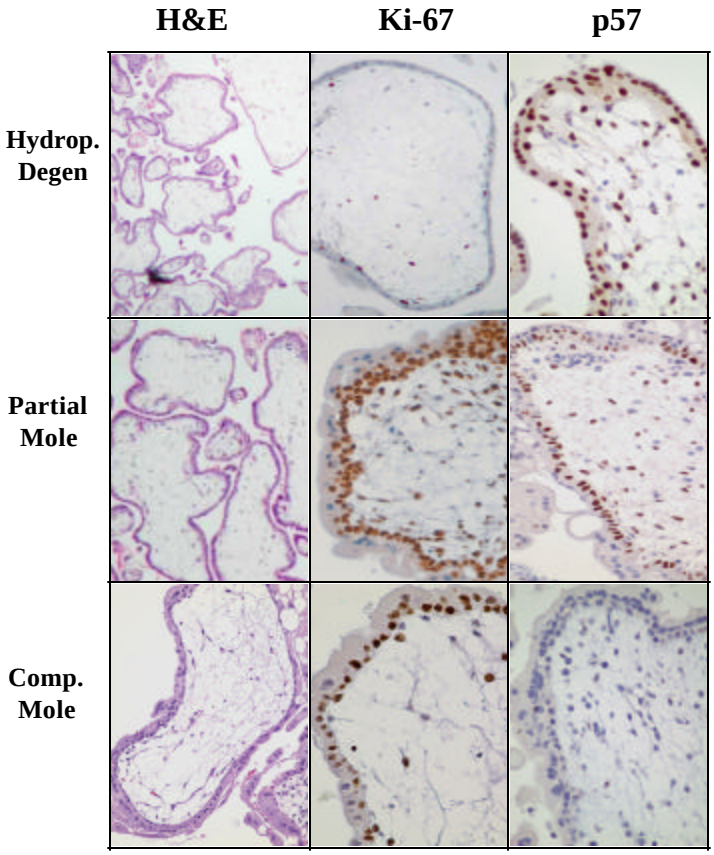
Microscopic examination of products of conception is a common task of many surgical pathologists. It is well known that on occasion it is difficult to distinguish degenerative changes in a nonmolar placenta (so-called "hydropic abortion") from partial hydatidiform mole and complete hydatidiform mole. Attesting to this fact is a 1993 study by Howat and associates that found 5 of 7 pathologists could reach diagnostic agreement in only 70% (35 of 50) of hydropic placentas when employing histologic criteria alone, underscoring the imperfect nature of the histologic criteria employed for distinguishing these entities. Particular difficulties were encountered in the identification of partial mole. Another study by Takahashi employing restriction fragment-linked polymorphism analysis discovered that 20% of 10 hydropic placental specimens were misclassified using histopathologic criteria. Because of differences in DNA content, DNA ploidy analysis by flow cytometry can assist in the accurate classification of these specimens, although those techniques may not be readily available in some locations. This month, we review several papers that discuss the utility of immunohistochemical stains for Ki-67 and $p57^{KIP2}$ in addressing this problem.

In a 1996 paper published in the International Journal of Gynecological Pathology, Schammel and Bocklage investigated the utility of P53, PCNA, and Ki-67 immunostains in distinguishing hydropic molar from nonmolar placentas. They studied 23 complete moles, 14 partial moles, 8 moles (not further classified), and 15 hydropic, nonmolar placentas. Diagnosis of each case was based on knowledge of both the histologic findings as well as the flow cytometry DNA ploidy data. PCNA and P53 expression did not allow accurate discrimination between molar and non-molar placentas. However, they found that Ki-67 immunostains differed significantly between the molar and nonmolar placentas. All partial or complete molar specimens contained at least one medium-sized villus that had >70% Ki-67-positive cytotrophoblastic cells rimming the periphery of the villi, whereas the maximum Ki-67 rim percentage (KRP) observed in the hydropic abortion specimens was 22%. We have employed KRP in this situation for several years, and we have found it useful in helping to separate such cases. It is important to adhere strictly to the definition of a "medium-sized villus", which is defined by the authors as a villus that just spans a 200X microscopic field using an Olympus microscope (20x objective with 10x ocular lenses). If this definition is not strictly adhered to, there may be a tendency to overdiagnose molar specimens. Ki-67 immunostains did not allow distinction of partial moles from complete moles, since both of these categories had a high KRP.

Recently, Castrillon et al and later Fukunaga reported that immunostains for $p57^{KIP2}$ protein, a cyclin-dependent kinase inhibitor, can assist in distinguishing diploid complete moles from diploid spontaneous hydropic abortions and triploid partial moles. Similar to normal placentas, diploid spontaneous hydropic abortions and triploid partial moles demonstrate a high frequency of expression of this protein in the nuclei of cytotrophoblasts, intermediate trophoblasts, and villous stromal cells (but not syncytiotrophoblasts). However,



H&E's of hydropic degeneration (left top), partial hydatidiform mole (left middle) and complete mole (left bottom) can look very similar. Corresponding Ki-67 immunostains are illustrated in the middle column and p57 immunostains in the right column. Note how the immunostain results allow a clear distinction among the entities.

complete moles show absent or low-level immunostaining in these same elements (low-level immunostaining was defined as 1-10% positive cells). Normal decidual stromal cells are strongly stained, serving as convenient internal positive controls.

By combining Ki-67 with p57^{KIP2} immunostaining, it is possible to accurately classify many of these specimens, using only these 2 immunostains. Hydropic abortions show a low Ki-67 KRP, but demonstrate high expression of p57^{KIP2}. Partial moles show a high KRP with high expression of p57^{KIP2}, and complete moles show high KRP with low expression of p57^{KIP2}. These results are summarized in the table below.

Obviously Ki-67 has been available for many years in the ProPath Immunohistochemistry Laboratory, but p57^{KIP2} is also now available for those who want to take advantage of this antibody to address this common problem in surgical pathology.

	Ki-67 Rim% (med size villi)	p57 in cytotrophoblasts & villous stromal cells
Hydropic Degen	Low (<22%)	High
Partial Mole	High (>70%)	High
Complete Mole	High (>70%)	Low

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