Diagnostic Value of Lectins in Differentiation of Molar Placentas

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Abstract

Objective(s)
Distinction of hydatidiform moles from non-molar specimens and subclassification of hydatidiform moles as complete and partial are important for clinical practice, but diagnosis based solely on histomorphology suffers from poor interobserver reproducibility. Nowadays, pathologists rely on molecular techniques, however these methods are technically difficult, relatively expensive, and time consuming, and cannot be applied in all laboratories. Therefore, a relatively easy, time- and cost-effective ancillary tool, would be helpful. This study aimed to assess the role of lectins in differential diagnosis of molar placentas.

Materials and Methods
Lectin histochemistry with a panel of HRP-conjugated lectins comprising SBA, DBA, MPA, PNA, VVA, UEA-1, LTA, GS-1 (B4), and WGA were performed in 20 non-molar (hydropic and non-hydropic spontaneous abortions) and 20 molar (partial and complete moles), formalin-fixed paraffin-embedded tissue samples. On the basis of staining intensity, sections were graded and Kruskal-Wallis non-parametric statistical test was used to compare differences between samples.

Results
There was a significant difference between the reactivities of LTA and UEA-1 with syncytiotrophoblasts of molar and non-molar specimens (P<0.001). These lectins generally showed a moderate reactivity with syncytiotrophoblasts of molar group but did not react with this cell population in non-molar group. Furthermore, WGA showed relatively increased reaction with syncytiotrophoblasts of molar tissues compared with abortions, however, this did not reach to statistical significance (P=0.07). No major differences were seen in other lectins reactivities between the studied groups.

Conclusion
The present study showed that UEA-1 and LTA lectins may be used as cytochemical probes in differentiating molar from non-molar placentas, but did not differentiate partial moles from complete moles.

Keywords: Diagnosis, Histochemistry, Hydatidiform mole, Lectins, Spontaneous abortion

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Lectin Histochemistry of Molar Placentas

Introduction
Gestational trophoblastic disease is a group of interrelated tumors originating from the placenta. Hydatidiform mole is the most common form of, which is an abnormal pregnancy characterized by hydropic swelling of placental villi and trophoblastic hyperplasia; this includes partial hydatidiform mole and complete hydatidiform mole (1).

Placentas characterized by hydropic swelling of chorionic villi occur in a spectrum of pathologic conditions including hydropic abortion, partial hydatidiform mole, and complete hydatidiform mole. Accurate diagnostic classification of hydropic placentas is important as the risk of persistent gestational trophoblastic disease is different among the three entities (2). Whereas hydropic abortion is completely benign, hydatidiform moles have a significant risk for developing persistent gestational trophoblastic disease, with a higher incidence in patients with complete hydatidiform mole (10-30%) than in patients with partial hydatidiform mole (0.5-5%) (3).

Histologic examination is the main tool in the diagnosis of molar pregnancies. However, there is considerable overlap in the histologic features between molar and nonmolar pregnancies and between complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM), resulting in significant interobserver and intraobserver variability in the diagnosis (4, 5). Recently, pathologists have relied on molecular techniques, such as DNA flow cytometry, chromosome in situ hybridization, and polymerase chain reaction-based genotyping or HLA typing, which by showing DNA content differences, help to correctly identify the hydropic placentas (6). However, the molecular methods are technically difficult, relatively expensive and time consuming, and cannot be routinely applied in all laboratories. Thus, a time- and cost-effective ancillary tool, available in most laboratories, would be helpful. Lectins are proteins or glycoproteins of nonimmune origin which are extracted from plants and animals. They have been used in many areas of diagnostic investigations, especially those related to changes in the expression of membrane and cytoplasmic glycoconjugates (7, 8). This study aimed to evaluate the use of HRP-conjugated lectins in differential diagnosis of hydropic placentas.

Materials and Methods
Case selection
Formalin-fixed, paraffin-embedded molar and non-molar placental tissue samples of some patients diagnosed in Departments of Pathology of Imam Reza and Qhaem, two teaching hospitals of Mashhad University of Medical Sciences, were collected. Molar tissue specimens consisted of complete hydatidiform mole (n=10) and partial hydatidiform mole (n=10). Non-molar tissue specimens consisted of spontaneous hydropic (n=10) and non-hydropic abortions (n=10). Mean value of gestational age was between 11-12 weeks. Tissue sections of the paraffin blocks were stained with routine hematoxylin-eosin and histopathologically reviewed for confirmation of diagnosis.

Lectin histochemistry
The paraffin blocks were cut into serial sections of 4-5 micrometer thickness and some sections were randomly stained with routine hematoxylin-eosin for selection of the best region for lectin histochemistry. Then, the selected sections of each group were deparaffinized in xylene and rehydrated through graded dilutions of ethanol. Endogenous peroxidase activity was blocked by preincubation of tissues with 0.5% hydrogen peroxide in methanol for 15 min at room temperature, and then washed in PBS. Tissue sections were covered with HRP-conjugated lectins (SBA, LTA, PNA, MPA, WGA, DBA, GS-I (B4), UEA-1, and VVA), which were purchased from Sigma-Aldrich company and diluted in 0.1 M PBS to reach final concentration of 10 μg of lectins, and placed in a humid chamber for 2 hr at room temperature. The tested lectins and their major sugar specificities are listed in Table 1. After incubation, excess unbound reagent was removed by washing 3 times in PBS and the reaction was then developed in 0.03% dianaminobenzidine in PBS with 0.006%...
hydrogen peroxidase and after 10 min, reaction was stopped by washing in tap water. The slides were counterstained with alcian-blue (1%) and then dehydrated and mounted in synthetic resin (9-11).

Negative control samples were made by the same procedure without lectins. For positive controls, human tissues were chosen for each lectin as indicated in the previous publications. Accordingly, normal term placenta was employed as the positive control tissue for WGA (12) and tissue sections of non-neoplastic colonic mucosa for SBA (12), colonic adenocarcinoma for PNA, VVA, and MPA (13, 14) and normal kidney for LTA, DBA, and UEA I (15) were used as positive controls. According to previous studies, in some experiments sialic acid was removed by pretreating the sections for 18 hr at 37 ºC in sodium acetate buffer 0.25 M, pH 5.5, containing 0.1 unit/ml neuraminidase, prior to application of PNA lectin (16, 17). All the slides were stained in the same batch to eliminate inter-batch variation. Ten fields were examined for each section using a light microscope (Olympus AH-2), magnification x200. The intensity of staining was graded subjectively by two observers. Each observer used a simple intensity scoring system, where negative indicated no staining, weak staining (light brown), moderate staining (brown), and strong staining (dark brown). Kruskal-Wallis non-parametric statistical test was used to compare differences between samples. The level of significance was defined at P<0.05.

Results
Reactivities to the lectins were assessed in villous cytotrophoblasts, syncytiotrophoblasts, and core stromal cells. The results are presented in Tables 2, 3, and 4, respectively.

Cytotrophoblasts
DBA reacted with cytotrophoblasts in molar and non-molar tissues, but no significant differences were observed among the studied groups. Other lectins did not react with cytotrophoblasts.

Syncytiotrophoblasts
SBA, DBA, VVA, and GS-I (B4) did not react with syncytiotrophoblasts of abortions and molar specimens. PNA also did not react with this cell...
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Table 1. Lectins used in this study and their major specificities (18, 29, 30)

| Name of lectin                  | Abbreviation | Major sugar specificity                      |
|---------------------------------|--------------|----------------------------------------------|
| Soybean Agglutinin              | SBA          | α/β-D-GalNAc > D-Gal                        |
| Dolichos biflorus Agglutinin    | DBA          | α-D-GalNAc                                   |
| Maclura Pomifera                | MPA          | α-Gal, α-GalNAc                              |
| Peanut Agglutinin               | PNA          | D-Gal (β1-3)-D-GalNAc GalNAc                |
| Vicia Villosa                   | VVA          | GalNAc                                       |
| Ulex europaeus Agglutinin I     | UEA I        | α-L-fuc                                      |
| Lotus Tetragonolobus            | LTA          | α-L-fuc                                      |
| Griffonia simplicifolia         | GS-I (B4)    | α-Gal                                        |
| Wheat Germ Agglutinin           | WGA          | (GlcNAc)n, Sialic Acid                      |

Abbreviations: CHM: Complete molar pregnancy, PHM: Partial molar pregnancy, HA: Hydropic abortion, Non-HA: Non-hydropic abortion, N: Negative, W: Weak, M: Moderate, S: Strong

Table 2. Intensity of lectins in villous cytotrophoblasts (%)

| Lectins      | CHM | PHM | HA | Non-HA | P-Value |
|--------------|-----|-----|----|--------|---------|
|              | N   | W   | M  | S      |         |
| SBA          | 100 | 0   | 0  | 0      |         |
| DBA          | 0   | 0   | 90 | 10     | 1.00    |
| MPA          | 100 | 0   | 0  | 0      | 0.58    |
| PNA          | 100 | 0   | 0  | 0      | 1.00    |
| PNA-N        | 100 | 0   | 0  | 0      | 1.00    |
| VVA          | 100 | 0   | 0  | 0      | 1.00    |
| UEA-I        | 100 | 0   | 0  | 0      | 1.00    |
| LTA          | 100 | 0   | 0  | 0      | 1.00    |
| GS-I         | 100 | 0   | 0  | 0      | 1.00    |
| WGA          | 100 | 0   | 0  | 0      | 1.00    |

Table 3. Intensity of lectins in villous syncytiotrophoblasts (%)

| Lectins      | CHM | PHM | HA | Non-HA | P-Value |
|--------------|-----|-----|----|--------|---------|
|              | N   | W   | M  | S      |         |
| SBA          | 100 | 0   | 0  | 0      | 1.00    |
| DBA          | 100 | 0   | 0  | 0      | 1.00    |
| MPA          | 20  | 80  | 0  | 0      | 0.85    |
| PNA          | 100 | 0   | 0  | 0      | 1.00    |
| PNA-I        | 0   | 0   | 70 | 0      | 0.94    |
| VVA          | 100 | 0   | 0  | 0      | 1.00    |
| UEA-I        | 0   | 0   | 90 | 10     | <0.001  |
| LTA          | 0   | 0   | 80 | 20     | <0.001  |
| GS-I         | 100 | 0   | 0  | 0      | 1.00    |
| WGA          | 0   | 0   | 20 | 80     | 0.07    |

Abbreviations: CHM: Complete molar pregnancy, PHM: Partial molar pregnancy, HA: Hydropic abortion, Non-HA: Non-hydropic abortion, N: Negative, W: Weak, M: Moderate, S: Strong.
population, but after neuraminidase treatment (PNA-N), a relatively moderate reactivity was observed in all of groups, which was most pronounced in apical portion. There was a significant difference between the reactivities of LTA and UEA-I with syncytiotrophoblasts of molar and non-molar specimens (P<0.001). These lectins generally showed a moderate reactivity with syncytiotrophoblasts of molar group but did not react with this cell population in non-molar group. WGA showed relatively increased reaction with syncytiotrophoblasts of olar tissues compared with abortions, however, this did not reach to a statistical significance (P=0.07).

**Core stromal cells**

All of the used lectins except VVA, reacted with core stromal cells. There were no significant differences in the reactivities of lectins between various groups.

**Discussion**

The present lectin-binding analysis of hydropic placentas was undertaken to identify possible new diagnostic markers that could be used in differential diagnosis of molar from non-molar hydropic placentas.

There have been several studies on the lectin-binding properties of chorionic villi in normal pregnancies, however, their findings are different (12, 19-21). We found a few studies about lectin-binding properties of molar pregnancies and spontaneous abortions. In the present study, for detection of the fucosyl residue, two different types of lectins, UEA I, and LTA, were employed. Reactivity with LTA suggests the presence of reactive sites containing α-L-fucose which bind via α(1-6) linkage to penultimate glucosaminyl residues and/or difucosylated oligosaccharides (22) while reactivity with UEA I, indicates the presence of α-L-fucose bound via β1,2 linkage to penultimate D-galactose-(β1-4)-N-acetyl-D-glucosamine residues (23). In molar group (partial and complete), LTA and UEA I, reacted moderately with syncytiotrophoblast which was prominent in apical portion, thus revealing the presence of α-L-fucose with both types of linkage, while in non-molar group (hydropic and non-hydropic abortions) no reaction with these lectins was seen in this cell population. The apical portion of the trophoblast corresponds to the microvillous brush border that has been shown to be heavily glycosylated in previous studies (24, 25). The brush border of the syncytiotrophoblast layer of the placenta forms the first barrier separating the maternal blood from the fetal circulation and is important in the exchange of nutrients, hormones, and waste products between the mother and the fetus. It is likely that the syncytiotrophoblast brush border plays a major role in the development of maternal immune tolerance (26). In previous studies on the human normal placenta, neither of these lectins reacted with the trophoblast (19, 20, 27). However, Sgambatti et al reported the

| Lectins | CHM | PHM | HA | Non-HA | P-Value |
|---------|-----|-----|----|--------|---------|
|         | N   | W   | M  | S     | N       | W   | M  | S     | N       | W   | M  | S     | P-Value |
| SBA     | 0   | 0   | 70 | 30    | 0       | 0   | 70 | 30    | 0       | 10  | 30 | 60    | 0.38    |
| DBA     | 0   | 10  | 60 | 30    | 0       | 10  | 60 | 30    | 0       | 10  | 40 | 60    | 0.26    |
| MPA     | 0   | 90  | 10 | 0     | 10      | 80  | 10 | 0     | 20      | 80  | 0  | 0     | 0.45    |
| PNA     | 0   | 10  | 0  | 80    | 0       | 0   | 80 | 0     | 0       | 10  | 90 | 0     | 0.27    |
| PNA-    | 0   | 0   | 80 | 20    | 0       | 0   | 90 | 10    | 0       | 10  | 80 | 10    | 0.73    |
| VVA     | 100 | 0   | 0  | 0     | 0       | 10  | 0  | 0     | 0       | 10  | 0  | 0     | 1.00    |
| UEA-I   | 0   | 0   | 0  | 80    | 0       | 0   | 90 | 10    | 0       | 10  | 90 | 0     | 0.35    |
| LTA     | 0   | 10  | 0  | 80    | 0       | 0   | 10 | 80    | 0       | 10  | 90 | 0     | 0.54    |
| GS-     | 0   | 0   | 100| 0     | 0       | 10  | 90 | 0     | 0       | 10  | 90 | 0     | 0.79    |
| WGA     | 0   | 80  | 0  | 20    | 0       | 0   | 90 | 10    | 0       | 80  | 20 | 0     | 0.92    |

Abbreviations: CHM: Complete hydatidiform mole, PHM: Partial hydatidiform mole, HA: Hydropic abortion, Non-HA: Non-hydropic abortion, N: Negative, W: Weak, M: Moderate, S: Strong
reaction with LTA and UEA I lectins observed in apical portion of syncytiotrophoblasts of normal placenta which increased during the late stage of placentation, whereas no binding of these lectins was seen in trophoblasts of human placenta of pregnancies complicated by intrauterine growth retardation which suggests the role of α-L-fucose in nutrient transfer (17). In this study, the moderate reactivity of syncytiotrophoblasts with LTA and UEA I, may be due to increased growth and proliferation of trophoblast in molar pregnancies which demand more exchange of nutrients and metabolic products. Our findings are discordant with the study done by Thrower et al who detected no binding of UEA I lectins to molar villous syncytiotrophoblast (28). Proteolytic treatment of paraffin sections done in this study affects lectin histochemistry (29), on the other hand, different detection methods may affect the results of lectin histochemistry (they used biotinylated lectins in their studies).

Increased WGA binding in syncytiotrophoblast of molar group compared with non-molar group could be due to increased N-acetylglucosamine and/or sialic acid. However, Tatsuzuki et al demonstrated that the brush border of syncytiotrophoblast layer of human term placenta strongly expressed GlcNAc and weakly expressed sialic acid (21). This is consistent with previous study done by Juan et al who showed that this increased reactivity was correlated with growth and proliferation of trophoblasts in trophoblastic disease (16). However, their study did not include spontaneous abortions and they used biotinylated lectins. In contrast, Thrower et al showed a weak reactivity in syncytiotrophoblast of all examined specimens comprising normal term pregnancy, ectopic pregnancy, and molar pregnancies, using WGA lectins. As described above, this may be due to different detection method or using of proteolytic treatment.

In the present study, as described in some previous studies (21, 30), PNA did not bind with villous syncytiotrophoblast and cytotrophoblast prior to neuraminidase treatment. However, after pretreatment with neuraminidase, the villous syncytiotrophoblasts showed moderate binding with PNA in molar and non-molar groups similar to previous studies (16, 17, 19). PNA lectin has been shown to have specificity for D-Gal (1-3)-D-GalNAc which is supposed to be the antigenic determinant for the Thomsen-Friedenreich antigen or TF-Ag (28, 29). This antigen is normally present in many structures. Ritcher et al reported expression of this antigen on trophoblast cells (31), but is considered cryptic, because it is usually covered by a terminal sialic acid. Pretreatment of tissue section with neuraminidase prior to application of PNA lectins will expose this T-Ag as was shown in the normal placenta (16).

All of the lectins except VVA reacted with villous stroma of both examined groups. This concurs with previous studies done in molar pregnancies (16) and normal placenta (17). However, Lee and Damjanov (19) reported that VVA reacted with stroma of normal placenta. There were no major differences in MPA, DBA, SBA, VVA, and GS-I (B4) reactivities with cytotrophoblast and syncytiotrophoblast of both molar and non-molar groups.

**Conclusion**

The results of this study suggest that lectin histochemistry can be used as an aid in the differential diagnosis of molar from non-molar hydropic placentas. Moreover, UEA-1, LTA and WGA lectins may be used as cytochemical probes in differentiating molar from non-molar placentas, but did not discriminate partial moles from complete moles.

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References
1. Soper JT, Mutch DG, Schink JC and American College of Obstetricians and Gynecologists. Diagnosis and treatment of gestational trophoblastic disease. ACOG Practice Bulletin No. 53. Gynecol Oncol 2004 Jun; 93(3): 575–585.
2. Berkowitz RS, Goldstein DP. Diagnosis and management of primary hydatidiform mole Obstet Gynecol. Clin. North Am 1988; 15:491–503.
3. Soper JT. Gestational trophoblastic disease. Obstet Gynecol 2006; 108:176-187.
4. Howat AJ, Beck S, Fox H et al. Can Histopathologists Reliably Diagnose Molar Malignancy? J Clin Pathol 1993; 46: 599-60.
5. Fukunaga M,Katabuchi H,Nagasaka T,et al. Interobserver and intraobserver variability in the diagnosis of hydatidiform mole, Am J Surg Pathol 2005;29:942-947.
6. Crips H, Burton JL, Stewart R, Wells M. Refining the diagnosis of hydatidiform mole: image ploidy analysis and p57KIP2 immunohistochemistry. Histopathology 2003; 43:363–373.
7. Walker RA. The use of lectins in histopathology. Pathol Res Pract 1989; 185:826-35.
8. Pilobello K, Mahal BK. Lectin microarrays for glycoprotein analysis. Methods Mol Biol 2007; 385:193-203.
9. Fazel AR, Schulte BA, Spicer SS. Glycoconjugate unique to migrating primordial germ cell differs with Genera. Anat Rec 1990; 228:177-184.
10. Fazel AR, Thompson R.P, Shumida H, Schulte BA. Lectin histochemistry of the embryonic heart: expression of terminal and penultimate galactose residues in developing rats and chicks. Am J Anat 1989; 198:85-94.
11. Ebrahimzadeh Bideskan AR, Hassanzadeh Taheri MM, Nikravesh MR, Fazel AR. Lectin histochemical study of vasculogenesis during rat pituitary morphogenesis. Iran J Basic Med Sci Jan-Feb 2011;14(1):35-41.
12. Nasir E, Lalani M, Bulmer JN, Wells M. Peroxidase-labeled lectin binding of human extravillous trophoblast. Placenta 1987; 8:15-26.
13. Cooper HS. Peanut lectin binding sites in large bowel carcinoma. Laboratory investigations 1982; 47:383-388.
14. Itzkowitz S H, Yuan M, Montgomery C K, Kjeldsen T, Takahashu H K, Bigbee W L. Expression of Tn, sialosyl-Tn and T antigen in human colon cancer. Cancer Res 1989; 49:197-204.
15. Silva F G, Nadasdy T, AND Laszik Z. Immunohistochemical and lectin dissection of the human nphron in health and disease. Arch Pathol Lab Med 1993; 117:1233-1239.
16. Juan FT, Hoshina AM, Mochizuki M. Lectin binding in tissues from hydatidiform mole, invasive mole and choriocarcinoma to cancavalin A, wheat germ agglutinin and peanut agglutinin. Asia Oceania J Obstet Gynecol 1989 Dec; 15(4):383-93.
17. Sgambaria E, Biagiotti R, Marini M and Brizzi E. Lectin histochemistry in the human placenta of pregnancies complicated by intrauterine growth retardation based on absent or reversed diastolic flow. Placenta 2002; 23:503-515.
18. Bancroft JD, Gamble M. Theory and Practice of histological techniques. 7th ed. London: Churchill Livingstone; 2008.
19. Lee MC and Damjanov I Lectin histochemistry of human placenta. Differentiation 1984; 28: 123–128.
20. Jones CJP, Dantzer V, Leiser R and Krebs C. Localisation of glycans in the placenta: a comparative study of epitheliolochoial, endotheliochoial, and haemomonochorial placentation. Micr Res Techn, 1997; 38: 100–114.
21. Tatsuzuki A, Ezaki T, Makino Y, Matsuda Y, Otha H. Characterization of the sugar chain expression of normal term human placental villi using lectin histochemistry combined with immunohistochemistry. Arch Histol Cytol 2009; 72(1):35-49.
22. Goldstein IJ and Poretz RD. Isolation, physicochemical characterization and carbohydrate-binding specificity of lectins. In The lectins, properties, functions and application in biology and medicine (Eds) Lierner IE, Sharon Nand Goldstain IJ London: Academic Press 1986; pp. 35–347.
23. Schulte BA and Spicer SS. Histochemical evaluation of mouse and rat kidneys with lectin horseradish peroxidase conjugates. Am J Anat 1983; 168: 345–362.
24. Whyte A. Lectin binding by microvillous membranes and coated-pit regions of human syncytiotrophoblast. Histochem J 1980; 12: 599–607.
25. Jones CJP, Dantzer V, Leiser R and Krebs C. Localisation of glycans in the placenta: a comparative study of epitheliolochoial, endotheliochoial, and haemomonochorial placentation. Micr Res Techn, 1997; 38: 100–114.
26. Truman P, Ford HC. The brush border of the Human term placenta. Biochimica et Biophysica Acta 1984; 779:139-160.
27. Lang I, Hartmann M, Blaschitz A, Dohr G, Skofitsch G and Desoye. Immunohistochemical evidence for the heterogeneity of maternal and fetal endothelial cells in human full-term placenta. Cell Tissue Res 1993; 274:211–218.
28. Thrower S, Bulmer JN, Griffin NR and Wells M. Further studies of lectin binding by villous and extravillous trophoblast in normal and pathological pregnancy. Int J Gynecol Pathol 1991; 10: 238–251.
29. Jeffrey IJM, Mosley SJ, Jones CJP, Stoddart RW. Proteolysis and lectin histochemistry. Histochem J 1987;19:269-75.
30. Sgambati E, Marini M, Vichi D, Zappoli G, Parretti E, Mello G, Gheri G. Distribution of the glycoconjugate oligosaccharides in the human placenta from pregnancies complicated by altered glycemia: lectin histochemistry. Histochem Cell Biol 2007; 128:263–273.
31. Richter DU, Jeschke U, Makovitzky J, Goletz S, Karsten U, Briese V, et al. Expression of the Thomsen–Friedenreich (TF) antigen in the human placenta. Anticancer Res. 2000; 20:5129-5133.